April, 1929.

BRAIN.

PART 1, VOL. 52.

HEPATO-LENTICULAR DEGENERATION; A FINAL NOTE.

BY STANLEY BARNES AND E. WESTON HURST.

In a former communication to this Journal [1] we described a group of four cases, three of which had been demonstrated at the Neurological Section of the Royal Society of Medicine in January, 1924 [2]. A further note in this Journal [3] recorded the final results after the death of the third patient; this communication completes the record of the fourth patient (Daniel B.), who died at the age of 11 in the General Hospital, Birmingham, on August 19, 1928.

Daniel B. was first examined in 1923, when he was 6 years of age, attention having been directed to the family by reason of a brother and sister both having shown signs of lenticular degeneration. At that date, it was found that he had an enlarged and hard liver, but that he was in no way inconvenienced by his abnormality, and no evidence of nervous disease could be obtained.

At the age of 7½, he had a severe attack of diarrhœa and vomiting, associated with fever of moderate degree, and lasting for several days. He probably became lightly jaundiced in this attack, but no observation by a reliable observer is available on this point. He made a complete clinical recovery from this attack, and remained in fair but impaired health for the next three years. The impairment in health was of a general character; he did not grow so rapidly as he should, nutrition was poor and lassitude of an unusual degree for a boy of his age was a predominant characteristic. For much of this period he was kept away from school, and this doubtless accentuated his mental backwardness. Nevertheless, those suggestions of choreic or athetoid movements of limbs and face which had been noted previously (see *Brain*, 1926, vol. xlviii, pp. 309-311) never advanced to such a degree that they could be recognized as beyond the limits of the normal; they appeared to express a personal eccentricity rather than evidence of organic disease.

In June, 1928, his abdomen began to swell, and he was again admitted to hospital on July 9, remaining there until his death on August 19, 1928.

On readmission (aged 11), he was poorly nourished, had a sallow complexion, but no jaundice. The abdomen was tightly distended with free fluid, and respiration was somewhat embarrassed. He lay placidly in bed, took an

intelligent interest in his examination, and answered questions correctly if somewhat slowly. No spontaneous movements were present, and on voluntary movement no chorea or athetosis was observed.

No pigmentation of the Kayser-Fleischer type was to be found on careful examination with a lens, but the slit lamp was not used on this occasion.

On July 17 he was tapped, and 190 oz. of clear straw-coloured fluid removed. Even after this was done, neither liver nor spleen could be palpated during deep inspiration. On July 21, the abdomen was beginning to fill up again, and slight jaundice was noted; a second paracentesis (210 oz.) became necessary on July 30, and thereafter he had some pain and tenderness over the liver region. Further tapping of the abdomen became necessary on August 14 (300 oz.), and it was noted that he was getting much weaker, more listless and drowsy.

During the night of August 16-17, he became mildly delirious and complained of abdominal pain, and on the morning of the 17th was semi-conscious and had incontinence of urine. Throughout the day at intervals of ten to fifteen minutes he suffered from tetanic spasms affecting chiefly the upper part of his body. "He would give a sudden cry, almost like a meningitic cry, and his mouth would be drawn up resembling a risus sardonicus, with some degree of head retraction. The arms, and to some extent the legs, would perform definite athetoid movements." (Note by the house physician). Between the attacks he lay in a semi-flexed attitude, relaxed, and on his side, speech being unintelligible except for occasional utterances.

The attacks continued, and as he appeared to be *in extremis* and in great distress, opium was given; the restlessness and tetanic attacks subsided for several hours, but at 2 a.m. on August 18 he again became restless, gave a sudden loud cry, and died almost immediately.

Throughout the period of six weeks during which he was in the hospital, the temperature never remained normal. There was as a rule a variation of one and a half degrees between his morning (lower) and evening temperatures. The highest recorded was on July 15, when it reached 101·2° F., whilst on several occasions it was as low as 97° F. It was an irregular hectic temperature of moderate degree, and during the last twenty-four hours varied between 100° F. and 98° F. No clinical cause, other than such as might be attributed to his liver disease, could be discovered for his fever.

The post-mortem examination was made six hours after death. The following are the notes made by Dr. F. W. M. Lamb, Assistant Pathologist, General Hospital, Birmingham:—

The body is that of an emaciated boy, aged 11.

The abdomen was distended with fluid of greenish-yellow colour, containing flakes of fibrin, but otherwise translucent and somewhat gelatinous. About three pints altogether were taken from the abdomen. Each pleura contained rather less than a pint of clear yellow fluid.

The skin showed a general sallow tint, probably icteric.

The conjunctivæ also showed a slight but general icteric tint.

The heart weighed about 200 grm., and showed no gross abnormality except for some pallor of the muscle, and yellow staining of the endocardium. The epicardium showed several petechial hæmorrhages.

Lungs: Slightly œdematous with yellow fluid (jaundice). Terminal hypostatic pneumonia.

Liver: 650 grm. Small, extremely atrophic and fibrotic. Areas of yellow (bile-stained) hyperplastic liver tissue separated from each other by strands of dense white fibrous tissue. Typical so-called "multilobular" cirrhosis.

Kidneys: 270 grm. No gross abnormality.

Spleen: 330 grm. large. Marked congestion of some duration, probably result of portal congestion.

Stomach, small and large intestines: No gross abnormality.

Pancreas: Appeared firmer than usual, but showed no trace of fibrosis.

Lymph glands at pylorus, along aorta, round pancreas, and in superior mediastinum, distinctly enlarged and congested.

Brain: Removed and preserved in 10 per cent. formol-saline, not cut except horizontally through outer part of hemispheres to allow penetration of formalin.

MICROSCOPICAL EXAMINATION. (E. W. H.)

The liver.—The appearances vary in different parts of the organ.

In many regions the liver is intersected by numerous bands of fibrous tissue attaining often a diameter of 2 mm. and subdividing the parenchyma into areas of comparatively large size (5 mm. diameter): in some instances partial subdivision of these large areas by much finer tracts of fibrous tissue occurs. Although in a few places near the edge of a lobule small groups of liver cells lie isolated by strands of connective tissue, on the whole the demarcation between the two is fairly sharp. The fibrous tissue shows a moderate number of small blood-vessels and new-formed bile-ducts; it is however not particularly rich in either. Areas infiltrated with round cells, occasional plasma cells and rare eosinophil leucocytes, occur.

In other regions the amount of fibrous tissue is greatly in excess of that of the parenchyma, which is represented by small masses rarely exceeding 1 mm. in diameter. Here the line of demarcation between liver and connective tissue is less definite and the liver cells are frequently split up into small groups by new-formed tissue. The formation at the periphery of the masses of numerous young bile-ducts of a less fully developed type than found elsewhere, the more intense round-cell infiltration and the scanty deposition of very delicate collagen fibrils, indicate that in such areas the destruction of liver tissue was actively progressing at or shortly before death.

Fatty degeneration of the liver cells is conspicuous in certain areas and plugs of bile-stained material can be seen in the fine bile capillaries or in the protoplasm of the secreting cells.

The nervous system.—Macroscopically no abnormality was detected.

The brain was subjected to an examination similar to that already recorded in our previous communications.

In the cortex the nerve cells were frequently slightly swollen with granular staining of the protoplasm and tiny vacuoles or a fine meshwork at the periphery. Such appearances were diffusely distributed and in no way confined to one area or cell-group of the nervous system; they were of the nature of acute changes ascribable to a terminal toxic state. Very occasionally a vessel in the subcortical white matter showed scanty perivascular infiltration with lymphocytes: not only was this occurrence rare, but it was never sufficiently marked to attract attention except on the closest examination. The glial cells were not obviously affected: no glial increase was evident and the peculiar Alzheimer cells seen in our previous cases were not present.

The lenticular nucleus, caudate nucleus and basal ganglia generally showed no definite pathological changes.

The brain-stem and cerebellum were normal.

The spinal cord was not examined.

The eyes.—Many sections were examined from both corneæ (the identity of which was unfortunately lost). One showed no pigmentation of any kind. The other contained a very few fine pigment granules situated not in Descemet's membrane but in some of the epithelial cells of the posterior surface. Over large stretches of this cornea the epithelium was devoid of granules, but occasionally groups of cells were seen containing tiny dark brown grains to the number of from one to six or eight in each cell. The staining reactions and solubilities of the pigment were those given by Hall as typical of the corneal deposits in hepato-lenticular degeneration, and not those of the pigment in our last case, which, it will be remembered, though confined to Descemet's membrane, differed from the usual in several particulars. It is difficult to decide whether this pigment, scanty in amount and atypical in situation, is on account of its reactions to be classed with the corneal pigment of other cases; it does not appear to be a formol precipitate.

One of the most remarkable features of this case (No. 4 of our series) is that in the final phase he should have exhibited a series of tetanoid attacks similar to those which were such a feature in the same stage of Case 1, although in the latter case clear clinical evidence of lenticular disease was present, whilst none could be obtained clinically or post-mortem in Case 4. Such a type of convulsion has not been observed by us before in cases of other forms of cirrhosis of the liver, when the moribund period is usually characterized by coma rather than convulsions, and when, if convulsions occur, they are of the epileptic type. It will be noted that in neither Case 1 nor Case 4 were the convulsions of the usual epileptic type, neither being accompanied by unconsciousness. The "fits" resembled the spasms of tetanus more than the crises of epilepsy, and were accompanied by evidence of fear, anxiety, sweating and severe pain. During the spasms an irregular form of decerebrate rigidity was developed, the precise form not being identical in the two cases.

It is difficult to give any adequate reason for the development of these spasms, especially as in the first case obvious gross changes were present in the putamen and cortex, whilst in the last one cortical changes of a very light type only were found. The suggestion, however, is put forward that:

(1) The patients both died during an attack of severe toxæmia.

(2) That during this period a large amount of toxin, untrapped by the damaged liver, flooded the nervous system.

(3) Widespread poisoning (and sudden temporary suspensions of function) occurred in various nuclear groups of the nervous system.

(4) The groups chiefly so affected were those which would ultimately have degenerated if the patient had not been previously killed by the severity of the liver disease, viz., the lenticular nucleus, and to a less degree the "middle level" cortex.

(5) The spasms would then be due to the unopposed activity of the "lowest level" innervation, the controlling effects of the lenticular nucleus and the "middle level" cortex having been temporarily abolished by the toxæmia, which left the "upper level" cortex substantially unaffected, whilst

(6) Death ensued when the "lowest level" and medullary group also ceased to function, partly owing to exhaustion from spasms, partly because the poisoning effect (toxæmia) had spread to these nuclei.

REFERENCES.

[1] Barnes and Hurst. *Brain*, 1925, **48**, 279.
[2] Barnes. *Proc. Roy. Soc. Med.*, Neurol. Sect., 1924, **17**, 34.
[3] Barnes and Hurst. *Brain*, 1926, **49**, 36.

A FORM OF MYASTHENIA GRAVIS WITH CHANGES IN THE CENTRAL NERVOUS SYSTEM.

BY DOUGLAS McALPINE, M.D.

(From the Pathological Laboratory of the Hospital for Epilepsy and Paralysis, Maida Vale, London.)

PAGE

1. Clinical Account of the Case 6
2. Pathological Findings 9
3. Significance of Mucocytic Degeneration 12
4. Myasthenia Gravis as a Possible Sequel to Epidemic Encephalitis 15
5. Discussion 20
6. Summary 21
7. Literature 22

This paper is based on a clinical and pathological account of a case of myasthenia gravis. Certain morbid changes were found in the central nervous system which have not previously been described.

Clinical Account of the Case.

G. E. H., a probationer nurse, aged 22, was admitted to the Hospital for Epilepsy and Paralysis, Maida Vale, London, on February 15, 1924, under the care of Dr. H. Campbell Thomson, who subsequently handed the case over into my care with a diagnosis of myasthenia gravis.

History.—The patient had enjoyed good health until October, 1923, when she noticed a slight difficulty in articulating certain words. A month later the lower limbs became weak after standing for any length of time. In December the arms were similarly affected. During the first week in January, 1924, she saw double for the first time. The patient particularly noticed that all her symptoms were more marked towards the evening, or after much exertion. In January she developed a right otitis media which was followed by an intermittent discharge from the ear. No history of insomnia, somnolence, pain or involuntary movements could be elicited. As far as the patient was aware she had had no rise of temperature, except possibly when the ear first discharged. There was nothing of importance in the family or personal histories.

Condition on February 18, 1924.—The patient appeared to be a

healthy young woman, though inclined to stoutness. She was intelligent and able to give a clear account of her illness. The pupils were equal and reacted well to light and accommodation. There was a slight but definite impairment of ocular movements in a lateral direction. Diplopia could be easily induced by asking the patient to perform repeated lateral movements of the eyes. Upward movement of the eyeballs was slightly restricted. Moderate bilateral ptosis was present, which varied in degree from day to day, but which was always more marked towards the evening. The facial muscles were bilaterally weak, more especially the orbicularis oculi. The circumoral muscles were less affected but the degree of paresis was sufficient to prevent the act of whistling, which had been possible before her illness. The masseters and temporal muscles contracted well and were not atrophied. The voice was considerably altered; it was feeble in tone and somewhat monotonous; at times dysarthria was marked, rendering her speech difficult of comprehension. The palate moved well on phonation but was easily fatigued. The tongue was protruded well and showed no atrophy or tremor; the patient had difficulty, however, in keeping it protruded for any length of time. The sterno-mastoid muscles and upper portion of the trapezii were not atrophied or weak, but both they and the extensor and flexor muscles of the neck tired easily.

Upper limbs.—Muscular atrophy was absent. Motor power was quite good, but repeated movements, especially at the shoulder, were quickly accompanied by lessened force and a subjective sensation of fatigue. The reflexes were brisk and equal on the two sides. There was no sensory loss.

Trunk.—No paresis of the abdominal or intercostal musculature could be detected. The abdominal reflexes were brisk and equal on the two sides.

Lower limbs.—Motor power was relatively good. The knee-jerks and ankle-jerks were brisk. In the case of the knee-jerk, taps on the patellar tendon repeated at short intervals resulted in a definite decrease in the degree of extension. Both plantar responses were flexor in type. There was no sensory loss. Gait was normal.

Electrical reactions.—A fairly typical myasthenic reaction was obtained in the fore-arm muscles.

Sphincters.—Control over these was normal.

Heart.—This was not enlarged and the heart sounds were normal.

Abdomen.—The liver and spleen were not enlarged.

Urine.—This was free from albumin and sugar.

Endocrine glands.—The thyroid gland did not appear enlarged. No definite enlargement of the thymus gland could be made out either by percussion or on X-ray examination. Menstruation was normal. There was no pigmentation of the skin and the blood-pressure figures were : Systolic 125, diastolic 75.

Ear, nose and throat.—There was a right otitis media, with a purulent discharge from this ear. The tonsils were enlarged and appeared septic.

Serological findings.—The blood Wassermann reaction was negative. The cerebro-spinal fluid was clear and was not under tension. The Wassermann reaction was negative. There were 3-5 cells per c.mm. and 0·035 per cent. of protein. The Lange gold curve was normal.

Progress.—Treatment of the otitis media was unsatisfactory, and on this account it was decided to remove the tonsils. These were dissected out on July 19. During many months in hospital her condition slowly grew worse. The muscular weakness in her limbs and elsewhere, which at first was only apparent after exertion, became permanent. The neck muscles, towards the end of her life, were considerably affected, so that at times, especially towards the evening, she was forced to support her chin with her hands. Dysarthria became permanent and latterly her speech was nearly incomprehensible. Dysphagia appeared about four months before death, and to this was added difficulty in mastication. Diplopia with partial external ophthalmoplegia were constantly present. The most distressing symptom, however, was dyspnœa, which was first noted in November, 1924. This occurred in attacks and was sometimes brought on by crying, which seemingly fatigued the diaphragm and intercostal muscles. The attacks lasted sometimes as long as four hours. The reflexes remained unaltered throughout the illness. On the morning of January 21, 1925, she had a severe attack of dyspnœa which persisted throughout the day with full retention of consciousness. Respiration was exceedingly shallow and difficult. Towards the evening she became comatose and died a few hours later.

Clinical summary.—A female, aged 23, developed dysarthria in October, 1923, followed a month later by diplopia. She readily became fatigued. These symptoms were always more marked towards the evening or after exertion. There was no history of sleep disturbance, pains or involuntary movements. When examined in February, 1924, she showed the following signs : A moderate bilateral and variable ptosis, diplopia and marked weakness of the orbicularis oculi and to a less extent of the lower facial musculature. Fatigue was easily

induced in the soft palate, tongue and limbs. The reflexes and sensation were normal. During many months in hospital her condition gradually grew worse; her symptoms were always worse towards the end of the day. Dysphagia, weakness of the neck muscles and permanent paresis of the limbs with attacks of dyspnœa became marked, and she died in a respiratory attack in January, 1925, her illness having lasted fifteen months.

Pathological Findings.

At the post-mortem examination, performed seven hours after death, no abnormality of the brain or spinal cord was noted. The thymus gland was much enlarged and weighed in the fresh state 48·5 grm. Parts of the following organs were removed for histological examination: thymus and thyroid glands, liver, spleen, kidney, suprarenal gland, uterus, Fallopian tube, ovary and heart. Portions of certain muscles were also removed, e.g., tongue, clavicular head of left sterno-mastoid, right external rectus, diaphragm, upper part of right trapezius, right biceps and deltoid.

Histological examination.—The various internal organs appeared normal with the exception of the thymus. The general structure of the gland was normal, but there was considerable increase in the depth of the cortex. The medulla contained about a normal proportion of Hassall's corpuscles. Owing to the kindness of Professor J. McIntosh, I was able to compare the sections with those from a young woman, aged 20, who suddenly died whilst dancing and in whom the only post-mortem finding of importance was an enlarged thymus gland. The histological appearances in the two cases were practically identical and pointed to a simple hypertrophy.

Numerous sections of the muscles mentioned above were carefully examined with completely negative results. No collection of cells resembling lymphorrhages were seen.

Nervous system.—The brain and spinal cord were fixed in a 10 per cent. solution of formalin. Various parts of the cortex, the basal ganglia and cerebellum were examined.

The brain-stem from the subthalamic region downwards was cut in serial section. Many sections of the spinal cord at various levels were studied. The methods used were: hæmatoxylin and van Gieson, hæmatoxylin and eosin, Nissl, Weigert-Pal, Loyez, Anderson's neuroglial stain, Scharlach R., Bielschowsky and Mayer's mucicarmine.

Cortex.—Sections from the frontal, rolandic, parietal and occipital

regions were examined. The cells of the various layers appeared normal. The vessels were normal except for deposits of mucin in the perivascular spaces. The Weigert-Pal preparations showed normal staining of the fibres, except when they were interrupted by mucocytes, which had pushed the fibres aside, leaving clear rounded spaces of varying size. The meninges were normal except for infiltration with mucoid material; this will be referred to later.

Basal ganglia.—The cells of the various nuclei appeared plentiful and the great majority were normal. There was no evidence of perivascular lymphocytosis. The fibres of the internal capsule stained well but were interrupted at frequent intervals by mucocytes of varying size.

Subthalamic region.—The various nuclei, such as the corpus Luysii, red nucleus, substantia nigra, tuber cinereum, and the nuclei in the neighbourhood of the third ventricle were normal, and no changes were seen in the vessels or neuroglial cells.

Brain-stem.—The nuclei of the cranial nerves were normal with the exception of the third nerve nucleus, a few cells of which showed some variation in their staining qualities but no definite evidence of chromatolysis. No intracellular lipoid material was seen. The vessels and meninges throughout the brain-stem were free from any cellular infiltration, except at the junction of the medulla and pons, where a small vessel showed a discrete perivascular lymphocytosis. Mucoid degeneration was present throughout the white matter of the brain-stem.

Spinal cord.—As the changes about to be described were similar in all parts of the cord, the following description of those present in the cervical region is applicable to other parts of the cord. The anterior horn cells were normal. The vessels showed well-marked perivascular infiltration with round cells. This was a striking feature in the majority of the sections examined, four to six rings of cells being commonly seen. The cells were sometimes arranged in the form of a cuff, similar to that seen in epidemic encephalitis. The majority of the cells were lymphocytes of medium size; their nuclei, containing a number of chromatin dots, stained well with hæmatoxylin. The nuclei varied in shape, some being rounded, others oval. Other cells present were small lymphocytes with a more deeply-staining nucleus, and hyaline endothelial cells with a large oval nucleus. Plasma cells were scarce. The perivascular infiltration was most marked near the postero-median fissure and in the region of the posterior root entry zone. In one or two sections cuffing was seen around a vessel in the anterior horn.

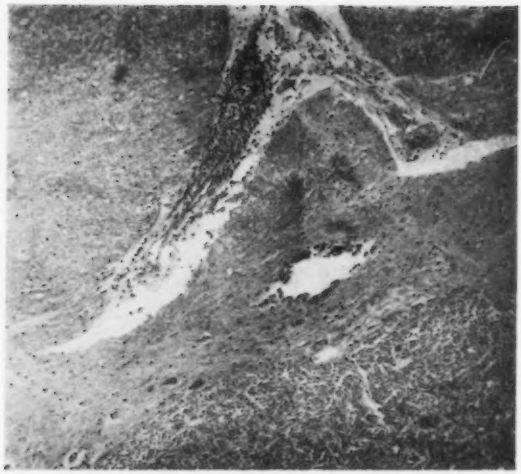


FIG. 1.—Section through mid-dorsal region of the cord, showing perivascular infiltration around a vessel in the antero-median fissure. Hæmatoxylin and eosin. x 60.

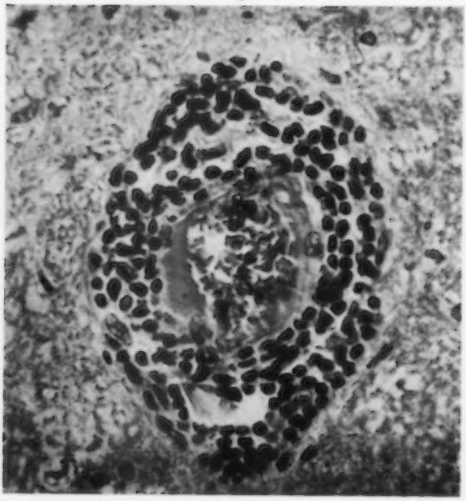


FIG. 2.—A section from the cervical enlargement, showing details of the perivascular infiltration. Hæmatoxylin and eosin. x 480.

FIG. 3.—Numerous mucocytes in the white matter of the spinal cord. Hæmatoxylin and van Gieson. x 50.

To illustrate Dr. Douglas McAlpine's paper.

Recent hæmorrhages into the grey matter of the anterior horns were observed in several sections, being absent from the brain-stem and brain itself. There was a slight but definite increase of neuroglial cells, chiefly around the anterior horns and posterior root entry zone. The meninges were normal except for deposits of mucoid material beneath them. In celloidin sections small and large mucocytes were numerous throughout the length of the cord.

Weigert-Pal sections showed no tract degenerations and were normal, except for a riddled appearance due to the mucocytes.

Mucoid Degeneration.

As deposits of mucin were extremely numerous, their character and disposition will be considered in more detail. In sections stained by the method of Nissl, especially when thionin blue was used, rounded or irregularly-shaped areas staining a faint pink colour were seen in the white matter. These areas were stained a bright blue colour with hæmatoxylin. The appearances in Weigert-Pal sections have already been described. The nature of this degeneration was made clear by staining sections with Mayer's mucicarmine, which gave a bright pink colour to the areas. This stain has been described as specific for mucin.

In a section through the cortex and adjacent subcortical white matter, the process was observed to be intense in the white matter. The vessels of the cortex itself were in many places surrounded by mucin. A diffuse infiltration of the meninges was observed in many places, and the process tended to invade the adjacent cortex. The general appearance of the degeneration in this region suggested that mucin was transported to the surface of the brain from the subcortical white matter through the agency of the perivascular lymphatics. The nuclei of the basal ganglia were relatively free, but vessels here and there contained mucin in their perivascular spaces. The internal capsule showed a great quantity of mucin scattered about in areas of varying size. Throughout the brain-stem the process was generalized, affecting chiefly the white matter. The degeneration in most places was at an early stage, the areas being comparatively small in size. The process extended up to the meninges and under the ependyma. The cortex of the cerebellum was unaffected, but in its white matter and the dentate nucleus the process was more marked than in the brain-stem or basal ganglia. In the spinal cord the degeneration was particularly intense. It was practically confined to the white matter

The areas varied considerably in size, some being quite large, due to fusion of several adjacent mucocytes. The mucoid material also tended to collect along the entering posterior root fibres.

Summary of Histological Findings.

The various visceral and endocrine organs were normal, with the exception of the thymus gland which was markedly hypertrophied. No lymphorrhages were observed in the muscles examined. The cerebral cortex, subcortical white matter and basal ganglia were normal apart from extensive mucocytic degeneration, which especially involved the white matter. The various motor nuclei in the brain-stem were unaltered except that a few of the cells of each third nucleus showed slight changes. The vessels were normal. Mucocytic degeneration was present. Many of the vessels of the spinal cord were markedly infiltrated with round cells. There was a slight degree of gliosis, especially around the anterior horns. The motor cells were normal at all levels. Mucocytes were more numerous in the cord than elsewhere. The meninges were normal.

THE SIGNIFICANCE OF MUCOCYTIC DEGENERATION.

Reference has been made to areas of mucoid degeneration. A review of the literature shows that this morbid change has attracted but little attention until quite recently. Buscaino [6], in studying brains from some cases of dementia præcox, found "grape-like areas" of disintegration in the white matter. He considered that these were the result of a true process of disintegration due to a lesion of the nerve fibres and neuroglial cells. Subsequently other workers on this subject found these "grape-like bodies" in a variety of pathological and even normal brains. It was shown that this form of degeneration was not apparent in frozen sections but only in those previously treated with alcohol or nitric alcohol. On this account Salustri [21], Ansalone [1], S. d'Antona [2] and others considered that they were artefacts. Lhermitte and Radovici [14], in cases of epidemic encephalitis, observed rounded areas with clear-cut edges, which stained red by the method of Casamajor, and violet-red by the method of Bonfiglio. The process was most marked in the white matter of the brain and spinal cord. It was sometimes observed in neuroglial cells, but more often it was extracellular and closely connected to the myelin sheaths. Grynfeltt [11], using Mayer's mucicarmine, was the first to recognize the nature of the degeneration and its origin in the interfascicular glial cells. He introduced the word "mucocyte" to indicate the cellular origin and chemical

nature of this form of degeneration. His work was based on the examination of a brain of an old man, but he gave no details as to the nature of the disease from which the man suffered. Lhermitte, Kraus and Bertillon [15] described fully the staining reactions of these "mucin-like bodies," which they observed in a case of post-encephalitic Parkinsonism, but denied their cellular origin.

Greenfield [9] observed the formation of mucin or mucinoid droplets in the bodies of interfascicular glial cells in epidemic encephalitis. He considered that the change may take place early, as he had observed it on the twenty-fourth day of the disease. Pélissier [20] studied this process in great detail in a case of chronic encephalitis. He described the distribution of mucocytes in the white matter throughout the brain, and stated that their presence in the grey matter can be explained by a migration of the mucocytes from the white matter. He also found mucoid material under the ependyma. He described in detail the formation of mucocytes from interfascicular glial cells.

Bailey and Schaltenbrand [3] observed this type of degeneration in a case of Schilder's disease. They adopted the term "mucocyte" as used by Grynfeltt and Pélissier, and proved that the interfascicular cells referred to by these authors are oligodendroglial cells. Grynfeltt and Pélissier showed that the mucin, formed for the most part in the white matter, found its way towards the surface of the brain on the one hand, and towards the ventricular cavities on the other. This migration appeared to be carried out through the agency of the perivascular lymphatic spaces.

Pagès, Bénoit and Pélissier [18] have deduced from these findings the possibility of mucin appearing in the cerebro-spinal fluid in certain diseases. The method which they used for the detection of this substance in the fluid is that of Derrien, the details of which are described in their paper. They have searched for mucin in 130 cases. In fifteen cases in which the fluid was withdrawn during spinal anæsthesia for various operations, no mucin was found. It was present, however, in a variety of organic neurological conditions, such as cerebral arteriosclerosis, epilepsy, dementia præcox and uræmia. It occurred most frequently in cases of chronic epidemic encephalitis.

Ferraro [8], in a recent critical review of the subject, based on his own work and that of others, came to the following conclusions:—

(1) The "grape-like body" of Buscaino and the mucocyte of Grynfeltt and Pélissier are identical.

(2) Their absence from frozen sections does not necessarily imply an

artefact, since the action of alcohol may reveal a form of lesion otherwise not apparent.

(3) The relationship between acute swelling of the oligodendroglia and the formation of mucocytes has not, in his opinion, been satisfactorily demonstrated. The absence of striking changes in the nuclei in the area of degeneration is a point against the origin of mucocytes from degenerated neuroglial cells.

I have attempted to repeat certain of Ferraro's experiments, but without any convincing results. The following are my conclusions, tentatively given: (1) Small rounded areas of mucin are present in frozen as well as celloidin sections of a large number of pathological conditions. No controls with normal material have been made. (2) In formalin-fixed material, which has been passed through celloidin, numerous irregularly-shaped areas corresponding to the large mucocytes of Grynfeltt and Pélissier have been found in the case of myasthenia gravis described in the present paper and in two cases of chronic epidemic encephalitis. These large mucocytes were absent from frozen sections both before and after treatment with alcohol for twenty-four hours. No attempt was made to determine the mode of formation or the origin of the small mucocytes, or the relationship between these and the large mucocytes of Grynfeltt and Pélissier. It seems obvious, however, that whatever their origin the presence of small mucocytes, owing to their frequency in morbid conditions of the brain and cord, is of little importance. On the other hand, the large mucocytes are in my experience much rarer, and may ultimately prove to be of considerable pathological interest.

Myasthenia gravis is a disease whose ætiology is at present unknown. No attempt will be made here to discuss the various pathological and biochemical theories that have been put forward from time to time to explain the curious phenomena so characteristic of the disease. An excellent summary of our present knowledge of the subject will be found in a recent paper by Keschner and Strauss [16]. The most constant pathological changes are collections of small round cells, resembling lymphocytes, in muscles, and certain visceral organs, to which Buzzard [7] gave the name of "lymphorrhages," and an enlargement of the thymus gland, which is hypertrophied or in some cases the seat of a tumour, usually benign. These two findings exist in about half the reported cases, although not always in association. According to the published accounts of the disease, changes in the central nervous system are rare. A number of different observers have noted varying degrees of

chromatolysis in the anterior horn cells of the cord. Buzzard, in one of his cases, found a few small collections of lymphocytes in the posterior root ganglia. Mandelbaum and Celler [17] described a lymphocytic infiltration around capillaries in the grey matter near the tenth nerve nucleus and ventral to the olivary body in one case. Barrada [4] laid emphasis on the presence of lipoid granules in the cells, especially of the thalamus and third nerve nucleus. Similar collections of lipoid material, however, are not uncommon in other pathological conditions. The above findings in the nervous system show no uniformity and are so relatively scarce that they can, I think, be safely disregarded in considering the ætiology of the disease.

Myasthenia Gravis as a Possible Sequel to Epidemic Encephalitis.

Such marked inflammatory and other changes in the spinal cord and brain as were present in this case suggest the possibility of an occasional relationship between epidemic encephalitis and myasthenia gravis. The association between these two conditions has been the subject of a few recent papers, and the case reports will now be considered in detail.

Grossman [10], in a paper entitled "Epidemic Encephalitis simulating Myasthenia Gravis," seems to have been the first person to draw attention to the possibility of this association. He described three cases in which the main symptoms and signs were a sudden appearance of diplopia with ptosis and varying degrees of ophthalmoplegia, dysarthria and dysphagia, an easily induced fatiguability of the limbs, and later the development of paresis and wasting, especially of the proximal musculature of the upper limbs. Two cases showed early bladder involvement and a doubtful plantar response, whilst one case exhibited choreiform movements. Grossman comments on the apparently acute onset of the illness, the lack of variation in the degree of muscular weakness, the absence of a myasthenic electrical reaction and the persistent ophthalmoplegia, as points against the diagnosis of a primary myasthenia gravis. On the other hand, the vesical disturbance and the doubtful plantar response in two of the cases suggested epidemic encephalitis. In one case that came to autopsy there was marked congestion of the vessels in the medulla with lesions of subacute inflammatory nature such as perivascular lymphocytosis and multiple hæmorrhages, most intense in the mid-brain.

Sarbo [22] cites the case of a male, aged 32, who had an attack of epidemic encephalitis in 1920. Bilateral facial paralysis with lethargy

lasting five weeks were the principal signs. Subsequently, he developed a rapid fatiguability of all his musculature. This was obvious during every movement, but disappeared if he lay down. The myasthenic electrical reaction was obtained on more than one occasion. No mention is made of the presence or absence of Parkinsonism. Paulian [19] describes a case occurring in a female, aged 29. In December, 1921, she was taken ill with fever and somnolence which lasted two months. This was succeeded by muscular weakness and intermittent diplopia, difficulty in walking, chewing and swallowing. Food regurgitated through her nose. The myasthenic electrical reaction was obtained. She presented the classical picture of myasthenia gravis, and this diagnosis was confirmed by several noted neurologists. She improved for a time, but, whilst abroad, she contracted pneumonia and died. The authors consider that the diplopia and somnolence at the onset pointed to an attack of epidemic encephalitis.

Wimmer and Vedmand [23] report two cases. The first was that of a male, aged 42, who was taken ill in October, 1918, with fever and somnolence. There were no ocular or other symptoms. The condition lasted for about three weeks. Within the next few months he noticed muscular fatiguability, nasal speech and dysphagia, followed by a falling of the lower jaw, which he was forced to support with his hand. In September, 1919, the speech became nearly unintelligible, after reading in a loud voice for one minute. The myasthenic electrical reaction was positive. In 1920, weakness in the arms was noted. He continued at work up till August, 1925, when he was compelled to enter hospital again. He showed atony and weakness of the facial musculature, and especially of the orbicularis oculi, with diplopia due to weakness of the left external rectus. There was atrophy of the masseters and tongue; the latter could not be protruded. Speech was indistinct and at times incomprehensible. There was a slight generalized wasting of the musculature of the limbs with a reduction in power. The faradic and galvanic electrical responses were lost in the masseters and temporal muscles, but no myasthenic reaction could now be obtained. During 1926 the patient improved.

The second case was that of a male, aged 40, who was taken ill with diplopia, muscular fatigue and bulbar symptoms. Somnolence and fever were absent. He improved, and continued at his work until August, 1924, when he noticed that his voice became weak after talking for a time, except in the morning. On examination he showed diplopia, inability to whistle, with marked weakness of the circumoral muscles.

There was no paresis of the vocal cords, but after reading aloud for about twenty minutes his speech became unintelligible. Dysphagia was also present. Motor power in the limbs was practically unimpaired, but fatigue could be easily induced. The deep reflexes were active and the plantar responses flexor in type. There was no myasthenic electrical reaction. The cerebro-spinal fluid was normal. During the next two years there were relapses and remissions in his condition, but in 1926 he was practically well except for an undue fatiguability of his voice. The authors base their diagnosis of epidemic encephalitis in the first case on the initial somnolence and fever. From their description of the cases it would seem possible that in the first case there was an attack of epidemic encephalitis. In the second case there is nothing incompatible with a diagnosis of myasthenia gravis *per se*.

Guillain, Alajouanine and Kalt [12] describe the case of a male, aged 57, who in January, 1925, developed diplopia, which at first was persistent, but later became transitory, appearing especially towards the evening or after fatigue. In October, 1925, variable ptosis, worse always towards the evening, pains in the lumbo-sacral region and fatigue in walking were noticed. Towards the end of a meal mastication became difficult, and there was a certain degree of dysarthria present. He had bilateral ptosis, paresis of the right external rectus and weakness of the masseters. Motor power in the limbs was normal except for a rapid fatiguability. The myasthenic electrical reaction was absent. In addition, the patient showed signs of a slight unilateral Parkinsonism. The second case was that of a male, aged 18, who was taken ill in December, 1922, with diplopia, bilateral ptosis and somnolence, which lasted three weeks. During the following months various myasthenic symptoms developed, such as an abnormal fatiguability of the limbs and masticatory muscles. There is no further note as to the outcome of this case. These authors conclude that in chronic encephalitis muscular weakness may develop, sometimes isolated, sometimes more or less generalized, appearing on or accentuated by muscular effort which closely resembles that seen in myasthenia gravis. Only a careful examination of muscular tonus and the absence of a myasthenic electrical reaction permit a differentiation between the two conditions.

Leenhardt, Reverdiget and Gondard [13] report the case of a boy of 13 in whom Argyll-Robertson pupils, ocular palsies, and double extensor plantar responses and rapid fatiguability of the muscles were noted. This case need not be considered on account of its general lack of resemblance to one of myasthenia gravis.

These few cases can be roughly divided into two groups: (1) Those in which the clinical picture of myasthenia gravis is well represented, but in which the occurrence of a previous attack of epidemic encephalitis is problematical: (2) those in which there is little doubt that the patient had an attack of epidemic encephalitis, but in which the condition that followed lacked several of the true myasthenic phenomena.

The cases described by Wimmer and Vedmand, and Paulian, would seem to fall into the first group, whilst the remainder correspond to the second group. Three points arise from a consideration of these cases:—

(1) Some of the authors lay stress on muscular atrophy as indicative of an underlying encephalitic infection, but in view of the fact that muscular atrophy is by no means rare in true myasthenia gravis, it is obvious that in this connection this sign should not be relied upon.

(2) In the majority of the case reports no mention is made of the presence or absence of paresis of the facial musculature. Wimmer and Vedmand's first case is an exception. It is well recognized that some degree of facial paresis is usual in the course of myasthenia gravis, the orbicularis oculi being most frequently affected, and therefore an intact facial musculature would be evidence tending to contradict the diagnosis of myasthenia gravis.

(3) Most of the authors lay considerable stress on the presence or absence of the myasthenic electrical reaction first described by Jolly. Although its presence is further diagnostic proof, its absence certainly does not militate against this diagnosis.

In reviewing the above cases it is evident that although there are some grounds for occasionally associating myasthenia gravis and epidemic encephalitis, pathological evidence is at present lacking in support of this.

In Grossman's second case, which came to autopsy, the clinical resemblance to myasthenia gravis, was very slight, the bulbar symptoms being terminal.

No case in the literature has been encountered in which there were inflammatory lesions mainly confined to the cord, and a clinical picture resembling myasthenia gravis such as were found in the present case. The nearest approach to such a case is one described by van Bogaert [5].

A male, aged 35, in December, 1925, first experienced dysarthria towards the evening or after much fatigue; this was accompanied by a feeling of constriction in the throat. Four weeks later these symptoms

had become aggravated, and movements of the tongue were now difficult. There was also dysphagia, especially with liquids. The patient also noticed a difficulty in holding up his head, and he became subject to attacks of dyspnœa. When examined in January, 1926, he showed definite atrophy and weakness of the circumoral muscles, tongue, masticatory muscles, and those of the neck. There was no fibrillary tremor, except in the tongue. The palatal reflex was present. Speech was bulbar in type and dysphagia was marked. The eyes were normal. No weakness of the limbs or alteration in the reflexes could be detected. There was no sensory loss on the face or limbs. Between January 1 and February 26, the condition gradually progressed, especially with regard to swallowing, speech and mastication. Paresis of the right arm developed, chiefly affecting the muscles of the hand, which showed commencing atrophy. The facial muscles *in toto* were now affected, and the circumoral muscles were so weak that food was retained in the mouth with difficulty. When examined on March 2, gross atrophy and weakness of the tongue and muscles of the face were noted. The speech was unintelligible. The hands presented the picture seen in the Aran-Duchenne type of atrophy. The deep reflexes were absent in the right arm and feebly present in the left. Walking was still possible, and the deep reflexes were conserved with normal plantar flexion. Death took place on April 17, five months from the onset. The main histological findings were: (1) The third nerve nucleus was normal. There was slight perivascular cuffing in the mid-brain. (2) In the pons many of the capillaries were congested. (3 In the dorsal portion of the medulla small neuroglial nodules were present in the neighbourhood of vessels. Perivascular lymphocytosis was present beneath the floor of the fourth ventricle. The twelfth nucleus, Roller's nucleus, the ventral nucleus of the seventh, and dorsal nucleus of the tenth nerve showed chromatolytic changes of varying severity. In the cord, especially in the cervical region, the vessels of the white matter were infiltrated with lymphocytes and plasma cells to a marked degree. The anterior horn cells were diminished in number; some of them showed chromatolytic changes. Weigert-Pal sections were normal. In the dorsal and lumbar regions of the cord the vascular lesions were less intense than at a higher level, and the motor cells were for the most part normal. The author points out that the pathological findings definitely exclude the diagnosis of an ordinary bulbar palsy, with progression of the disease caudally. He contrasts the localization of the inflammatory lesions in the cervical cord with the definite nuclear changes in the medulla. He describes another similar case in which death had not occurred.

Discussion.

(*a*) *Clinical.*—The clinical picture and course of the disease in the present case were considered typical of myasthenia gravis during the life of the patient. The case was seen by several of my colleagues from the point of view of treatment, and this diagnosis was always confirmed. The question of a possible antecedent attack of epidemic encephalitis was considered in the first instance, but no distinctive symptoms suggesting the acute phase of this disease could be elicited. The histological findings in the cord seemed to throw doubt on the validity of the diagnosis, and therefore the possible relationship of the case to epidemic encephalitis came to be considered. As we have seen, the clinical evidence for a myasthenic type of epidemic encephalitis is not very convincing, but at the same time one or two of the published cases are suggestive in this connection. If epidemic encephalitis does actually produce in some cases a picture of myasthenia gravis, one would have expected an increase in the number of cases of this disease. As far as I am aware, there is no published evidence in support of this view. Turning to the pathological side of the question, what interpretation can be placed on the inflammatory changes in the spinal cord? Assuming for the moment that these may be due to epidemic encephalitis, let us consider the clinical symptoms which may result from involvement of the spinal cord in this disease as proved at autopsy. In the first place, in those cases where the changes are widespread, affecting both brain and spinal cord, there may be no symptoms indicating a downward spread of the disease. In other cases, myoclonic movements and root pains are the expression of the cord lesions, and these symptoms may constitute the greater part of the clinical picture. In a much smaller group are found those cases in which histologically the disease has been practically confined to the cord, and in which the clinical picture is that of a myelitis or neuronitis.

It is evident then that the present case considered from the point of view of epidemic encephalitis does not fall into any previously described clinico-pathological group.

(*b*) *Pathological.*—Marked changes in the muscles and viscera were conspicuous by their absence, except in the case of the thymus gland which showed hypertrophy. If the changes in the central nervous system are to be accorded an important rôle in considering the pathogenesis of the present case, then the hypertrophy of the thymus gland must be considered of little account. Buzzard found lymphorrhages in all five cases of myasthenia gravis which he examined. Their absence

in the present case suggests the possibility that we are dealing with a type of myasthenia gravis which differs from the classical form. The importance of a careful examination of the muscles and viscera for lymphorrhages was emphasized by Buzzard; this was recognized at an early stage of the investigation of this case and the portions of muscles were in most instances cut in serial section.

When we come to consider the changes in the cord, the first point to be decided is the nature of the perivascular lymphocytosis. Is this comparable with lymphorrhagic invasion of muscles and visceral organs? The presence, however, of other types of cells besides lymphocytes, such as endothelial and plasma cells, accompanied by over reaction of the neuroglia, definitely points to an inflammatory process. Comparison of the sections with those from cases of subacute encephalitis showed that there was little difference between the character of the cells around the vessels. The significance of mucocytic degeneration which was such a marked feature, not only in the cord but in the brain, has already been alluded to. As far as the evidence provided by the literature goes, chronic epidemic encephalitis shows this form of degeneration more markedly than any other disease. In this connection it may be stated that the process was greater in this case of myasthenia gravis than in any of the cases of chronic epidemic encephalitis which were examined. Van Bogaert's case, referred to earlier in this paper, closely resembles the present one, both clinically and pathologically, except with regard to the muscular atrophy and the chromatolytic changes in the nuclei of the seventh, tenth and twelfth cranial nerves, and in the anterior horn cells of the cervical cord. These findings, which seem interdependent, were absent from my case.

Finally, a study of this case from every angle has forced me to the conclusion that there is a form of myasthenia gravis indistinguishable clinically from the classical type of this disease, associated with inflammatory changes in the cord, which may have a causal relationship.

I am indebted to Dr. J. G. Greenfield for several of the references dealing with the subject of mucocytic degeneration.

Summary.

(1) A case of myasthenia gravis is described in which inflammatory changes in the spinal cord with widespread mucocytic degeneration were found.

(2) The possibility of an occasional relationship between myasthenia gravis and epidemic encephalitis is considered.

(3) It is concluded from a study of the case that there is a form of myasthenia gravis associated with inflammatory changes in the central nervous system, the cause of which is at present problematical.

REFERENCES.

[1] Ansalone, G. "Contributo alla istologia patologica della demenza precoce," *Riv. sper. di freniat.*, 1924, **48**, 208.

[2] D'Antona, S. "Sulla genesi della cosi dette zolle di disintegrazione a grappolo," *Rassegna di stud. psichiat.*, 1924, **13**, 501.

[3] Bailey, P., and Shaltenbrand, G. "Die muköse Degeneration der Oligodendroglia," *Deutsch. Zeitschr. f. Nervenheilk.*, 1927, **97**, 231.

[4] Barrada, Y. A., and Mott, F. W. "Pathological Findings in the Central Nervous System of a Case of Myasthenia Gravis," *Brain*, 1923, **46**, 237.

[5] Van Bogaert, L. "Étude sur la paralysie labio-glosso-laryngée à évolution subaigue," *Rev. Neur.*, 1928, **35**, 69.

[6] Buscaino, V. M. "La cause anatomopatologische delle manifestazioni Schizofreniche nella demenza precoce," *Riv. di patol. nerv.*, 1920, **25**, 197.

[7] Buzzard, E. F. "The Clinical History and Post-mortem Examination in Five Cases of Myasthenia Gravis," *Brain*, 1905, **28**, 438.

[8] Ferraro, A. "Acute Swelling of the Oligodendroglia and Grape-like Areas of Disintegration," *Arch. of Neur. and Psych.*, 1928, **20**, 1065.

[9] Greenfield, J. G. "The Pathology of Epidemic Encephalitis," *Journ. of State Medicine*, 1926, **34**, 703.

[10] Grossman, M. "Epidemic Encephalitis simulating Myasthenia gravis," *Journ. of Ment. and Nerv. Dis.*, 1922, **55**, 32.

[11] Grynfeltt, E. "Mucocytes et leur significance," *Compt. Rend. et Mém. de Soc. de Biol.*, 1923, **89**, 1264.

[12] Guillain, G., Alajouanine, Th., et Kalt, M. "La forme myasthénique de l'encéphalite épidémique prolongée," *Rev. neurol.*, 1926, **33**, 39.

[13] Leenhardt, Reverdiget et Gondard. "Un cas de myasthénie postencéphalitique," *Bull. de la Soc. de Sci. Méd. de Montpelier*, 1927, **5**, 226.

[14] Lhermitte, J., et Radovici, A. "Étude sur la dégénération basophile metachromatique dans l'encéphalite épidémique," *Compt. rend. de la Soc. de Biol.*, 1921, **84**, 931.

[15] Lhermitte, J., Kraus, W. M., and Bertillon, F. "Mucin-like Bodies in the Central Nervous System in Epidemic Encephalitis," *Arch. of Neur. and Psych.*, 1924, **12**, 620.

[16] Kescher, M., and Strauss, I. "Myasthenia Gravis," *ibid.*, 1927, **17**, 337.

[17] Mandelbaum, F. S., and Celler, H. L. "A Contribution to the Pathology of Myasthenia Gravis," *Journ. of Exper. Med.*, 1908, **10**, 308.

[18] Pagès, M., Bénoit et Pélissier, G. "La dégénérescence mucocytaire de la Nevroglie," *Languédoc Médical*, 1926, **9**, 1.

[19] Paulian, D. E. "Considérations étiologiques sur la myasthénie et ses relations avec l'encéphalite épidémique chronique," *Rev. Neurol.*, 1926, **33**, 368.

[20] Pelissier, G. "Syndrome Wilsonien consécutif a la névraxite épidémique," *Thèse de Montpelier*, 1924.

[21] Salustri, E. "Sulle cosi dette zolle di disintegrazione a grappolo," *Rev. sper. di freniat.*, 1924, **48**, 255.

[22] Sarbo, A. "Ueber die Encephalitis epidemica, auf Grund der Erfahrungen der Epidemie von 1920," Abst. *Zeit. f. d. ges. Neur. u. Psych.*, 1921, **27**, 509.

[23] Wimmer, A., et Vedmand, H. "Le syndrome myasthénique dans l'encéphalite épidémique chronique," *Rev. Neurol.*, 1926, **33**, 368.

ARTERIOSCLEROTIC PARKINSONISM.[1]

BY MACDONALD CRITCHLEY.

CONTENTS.

		PAGE
CHAPTER I.	INTRODUCTION	23
CHAPTER II.	HISTORICAL	25
CHAPTER III.	SYMPTOMATOLOGY	32
CHAPTER IV.	MORBID PHYSIOLOGY	57
CHAPTER V.	PATHOLOGY	64
CONCLUSIONS ..	.. ..	78

CHAPTER I.—INTRODUCTION.

HITHERTO scant attention has been paid to the occurrence of Parkinsonism among the syndromes of cerebro-vascular disease. It is the object of this paper to emphasize the importance of this syndrome as being one of the most frequent objective manifestations of a protean disease. By the term Parkinsonism is here understood a condition of general rigidity of non-pyramidal type, with weakness and slowness of movement—in fact, a symptomatic variety of paralysis agitans such as one associates with disorder of the pallidal system. As we shall see, so-called " neostriatal manifestations " of the nature of athetosis, tremor, or chorea play little or no part in this variety of Parkinsonism.

It is not essential, nor indeed is it usual, to find the Parkinsonian syndrome in its entirety in cerebral arteriosclerosis. Incomplete forms are more common; thus one patient may show a generalized rigidity, another a poverty of spontaneous movement, and another a mask-like facies or bradykinesis. Cerebral arteriosclerosis is, however, a progressive malady and the clinical picture may change rapidly so that various incomplete forms often merge into an identical state of complete Parkinsonism.

The importance of this syndrome becomes evident when it is shown to take part in syndromes as diffuse as Marie's " état lacunaire," pseudo-bulbar palsy, cerebral meiopragia (Claude and Cuel [15]), "arterio-sklerotische Muskelstarre " (Foerster [25]), and many of the organic

[1] Work carried out at the National Hospital, Queen Square, with the assistance of the Medical Research Council.

psychoses. Parkinsonism of greater or lesser degree may be regarded as a common multiple, participating in syndromes of the utmost diversity.

The relationship between arteriosclerotic Parkinsonism and "senile" or "idiopathic" paralysis agitans is not easy to define, but there are certain clinical and pathological points of differentiation between them, as there are between the idiopathic and post-encephalitic varieties. A study of the literature and a wide experience of cerebral arteriosclerosis of all types make it obvious that many cases of symptomatic Parkinsonism would at first sight be relegated to the "idiopathic" group, and, secondly, seem to indicate that there is no sharp distinction between the so-called idiopathic and symptomatic types. The more detailed the clinical examination and the closer the study of the disease the narrower becomes the category of "idiopathic" paralysis agitans.

The trend of modern thought is to regard Parkinsonism as a syndrome rather than as a disease; such was the opinion of Souques [90] in 1921, when he said: "Paralysis agitans or Parkinson's disease is not in my opinion a disease-entity. I picture it as a syndrome common to different causes acting upon the same part of the brain. The important factor is not so much the nature of the cause as its site—not so much the variety of the lesion as its topography." Again, Foix and Nicolesco [25] adopt the same standpoint: "There are no absolute frontiers between Parkinson's disease—so-called—and the pseudo-bulbar Parkinsonism of the aged. There is no doubt in our mind that we will more and more place into their true category (i.e., Parkinsonism) certain symptoms of that type often met with in the aged."

Foerster's description of arteriosclerotic rigidity appeared in 1909, and it is obvious from his clear account that he was describing a variety of hypertonus which fulfils many of the requirements of so-called extrapyramidal rigidity. Other factors are present, however, which contribute to the state of increased tonus, but the basis is a pallidal type of rigidity. Foerster remarks on the close analogy with paralysis agitans, and suggests the possibility of an identical location of the disease. In the absence, however, of a sure anatomical basis, he writes in his concluding paragraph, "I must content myself for the present with describing this particular disease-picture as arteriosclerotic rigidity."

Although the arteriosclerotic varieties of Parkinsonism have not received widespread recognition, the symptomatic varieties resulting from vascular disease of syphilitic nature are well known. Mesencephalitis syphilitica (of Kinnier Wilson and Cobb) is an example.

The conception of a pallidal type of arteriosclerosis is familiar to continental writers, but in this country it is scarcely ever specifically mentioned, although possibly a matter of common experience. James [43] has described many of the Parkinsonian symptoms which occur in the late stages of severe cerebral arteriosclerosis, and he quotes Mott as saying that cerebral arteriosclerosis may be confused clinically with the sequelæ of encephalitis lethargica. The writings of C. and O. Vogt, Jakob, Steck, Lhermitte and his collaborators (to quote only a few) testify to the continental recognition of pallidal syndromes of arteriosclerotic origin. Souques has classified the clinical types of Parkinsonism as follows :—

(1) Presenile or senile Parkinsonian syndromes: (*a*) typical; (*b*) sine agitatione; (*c*) sine rigiditate.

(2) Juvenile Parkinsonian syndromes.

(3) Parkinsonian syndromes due to presenile lesions of the corpus striatum.

(4) Parkinsonian syndromes due to macroscopic focal lesions (e.g., lacunes).

(5) Post-encephalitic Parkinsonian syndromes.

The varieties included by Souques in his third and fourth categories are those which come within the scope of this paper.

Regarded from another angle this paper is intended as a contribution to recent studies in psychiatry wherein neurological features are studied in relationship to various psychoses. In association with the clinical and pathological studies of striatal factors in dementia præcox (Farran-Ridge [23], Stoddart [93], Reiter [87], Wladyezko [105]), in general paralysis (Steck [91]), in manic-depressive insanity (Urstein [96]), in Alzheimer's disease (Stief [92]), the problem of the involvement of the basal ganglia in senile and arteriosclerotic dementia merits attention.

Chapter II.—Historical.

The varieties of arteriosclerotic Parkinsonism do not permit of a sharply defined clinical classification. Such types as exist merge one into another, and in several instances the differences are in degree rather than in character. But for the sake of clarity and convenience in description it is advisable to attempt a classification. The following five varieties may be isolated :—

Type 1—characterized by rigidity, fixed facies, and short-stepping gait.

Type 2 as in Type 1, with the addition of pseudo-bulbar manifestations (dysarthria, dysphagia, spontaneous laughter and crying).

Two sub-types can be recognized: (*a*) cases with signs of pyramidal disorder, (*b*) cases without signs of pyramidal disorder.

Type 3 as in Type 1, but with the addition of dementia, and incontinence of urine and fæces.

Type 4 as in Type 1, with signs of pyramidal disease but without pseudo-bulbar manifestations (=mixed pyramido-pallidal syndrome).

Type 5 as in Type 1, but with the super-imposition of cerebellar symptoms (=mixed pallido-cerebellar syndrome).

It is obvious that a certain amount of overlap is unavoidable if the above classification is adopted. Thus, in Type 2 there may be signs of pyramidal disease, and in addition some degree of dementia and incontinence may be present.

The first type, which may be regarded as the mildest variety of Parkinsonism, is perhaps the commonest. As a rule the syndrome does not cause much incapacity, hence instances are encountered socially rather than professionally. Frequently the only symptoms are hyperpietic in type and the patient comes under observation for headache, giddiness, defect of memory, or frequency of micturition. Many of the patients described by Marie as "lacunaires" come into this group. Some of the severer examples would be included within Foerster's description of arteriosclerotic rigidity. Collins [78] (1906) refers to this type in his paper on "a definite variety of cerebro-vascular disease." In his series of 135 cases of arteriosclerosis this particular syndrome was present thirteen times. He also refers to a case reported by Pickett [78], of a man of 67 who had gradually become "stiff all over" in the course of two years. There was no mental enfeeblement; sphincter control was perfect; but the speech was "mumbling." A particular case had been described by Collins [16] himself in the previous year: A woman of 50 gradually changed in character and became subject to frequent local epileptic spasms confined to one hand. There was no paresis but a definite absence of elasticity or grace in her movements . . . "her appearance and attitude reminding one forcibly of Parkinson's disease." There were no changes in the reflexes.

The following case exemplifies the characteristic features of the first type:—

J. P., male, aged 66, came to the National Hospital (Dr. Walshe) because of difficulty in walking. For two and a half years he had gradually become uncertain on his legs, and complained of a tendency to fall backwards. He

noticed also that he was becoming slower in his movements. Examination revealed a well-nourished old man with a fixed and expressionless face. His attitude was statuesque and there was an obvious poverty of spontaneous movement: speech was a little monotonous and not well articulated. There was no psychical change. A generalized rigidity was noticeable in the trunk and extremities; muscular strength was good but all movements were performed slowly. Tremor was not present. All the tendon jerks were brisk; the plantar responses were flexor in type; no clonus was obtainable. When walking the patient held himself stiffly, swung his arms awkwardly at the shoulders, and took very short shuffling steps. Blood pressure was 218/105; the radial arteries were thickened, and the retinal arteries were tortuous and indented the veins. The second aortic sound was ringing.

Some of the cases recorded by Lhermitte [54] and [55] and by Verger [97], belong to this clinical group. Van Gehuchten's case [34] was similar but differed in the suddenness of onset. In Signorelli's patient [89] there was also a nystagmus of the palate, pharynx and vocal cords.

The second category includes those patients who show, besides the features characteristic of Type 1, manifestations of a "pseudo-bulbar" nature. The clinical picture is in fact that of a double hemiplegia, with or without a history of successive strokes, but with definite manifestations of a Parkinsonian nature. In a proportion of cases, probably in the majority, the Parkinsonian traits have been masked by the more obvious paretic signs, and have consequently not been directly emphasized. It is probable, too, that in the past some of these patients have been regarded as instances of "paralysis agitans with bulbar symptoms." (cf. Ashley Mackintosh [69]; Janischewsky [44].)

This group may be further subdivided according as to whether signs of pyramidal disease are demonstrable or not. In those cases which are sometimes tersely though inaccurately termed "double hemiplegics," Babinski responses, ankle clonus, and signs of pyramidal spasticity reveal a state of bilateral pyramidal disease. The majority of these have few Parkinsonian signs. Where a pseudo-bulbar syndrome exists without signs of pyramidal affection, the Parkinsonian manifestations are usually more obvious. The onset is usually gradual and there is frequently no history of a stroke. Typically, the patients in this group show no mental enfeeblement, though their emotivity may give rise to a false impression of childishness. In severer cases, however, some degree of dementia is present, and the case merges gradually into Type 3.

This particular syndrome was first commented on specifically by

Brissaud [9] (1895), as a characteristic clinical variety of senile softening. After detailing the features common to paralysis agitans and to the pseudo-bulbar syndrome, he pointed out the Parkinsonian attitude and physiognomy and described a short-stepping gait, slow and uncertain movement as commonplace features with subjects who had sustained numerous small softenings of thrombotic origin.

As an example of the type of patient included within Group 2 the following case may be quoted :—

B. T., female, aged 51, was admitted to the National Hospital (Dr. Holmes) for giddiness. Symptoms of general weakness and difficulty in walking had been present for eighteen months. She was dull mentally and emotionally very unstable. The speech was dysarthric. Her face was staring and immobile. There was no local paralysis : the tendon jerks were increased and the plantar responses were indefinite. All her movements were slow and there was an universal rigidity. She had some difficulty in swallowing fluids. Walking was a matter of great difficulty and was characterized by extremely small shuffling steps. Blood pressure was 225 130 ; the radials were hard and tortuous ; the second aortic sound was accentuated. Blood urea 30 mg. per cent. ; non-protein nitrogen 2·5. She was seen one year, and again eighteen months later in an Infirmary ; her physical signs were as before, with the addition of some degree of facial apraxia and over-reaction on emotional movements.

Numerous similar cases could be quoted from the literature. Cases R. E. and A. R. recorded by Holmes [38] belong to this category, but in these instances tremor was also present. A patient reported by Lemos (and afterwards pathologically by C. and O. Vogt) was described by him as suffering from a "paralysie pseudo-bulbaire Parkinsonienne." Other cases include those of Noethe [74], Monier-Vinard and Dalsace [71], Lhermitte and Cornil [57], Claude and Alajouanine [14], Verger [97], and Urechia, Mihalescu and Elekes [95]. All seven of Kashida's patients [46] and three of Kleist's (Nos. 1 and 6 [47] and No. 6 [48]) belong to this category.

Type 3 includes patients who present, in addition to Parkinsonian features, some degree of mental deterioration and incontinence of urine and fæces. The psychical changes range from simple retardation and defect of memory to the grossest varieties of global dementia. Sphincter disorders are always present, varying from the occasional lapses due to inattention to a complete lack of control over the excretions. A proportion of the patients in this category have signs referable to disordered bulbar function, but these are slight when compared with the preponderating psychical defects. Evidences of unilateral or bilateral

pyramidal affection are not rare, but they are slight and unessential in this particular syndrome.

Rowland (1851) [84] probably referred to this type when he wrote of the restless and demented arteriopath: "There is a species of mental imbecility sometimes accompanying cerebral softenings, which is manifested chiefly in the manner and actions, and on that account is called by the French physicians "délire d'action." . . . From this state they generally pass into more determined dementia, in which the mind is hopelessly clouded, the expression vacant and idiotic, while, at the same time, the extremities are paralytic."

The following case illustrates the main clinical features characteristic of the third type:—

H. C. H., male, aged 72, was seen on several occasions at St. Pancras Infirmary. No history was obtainable. His mental state was one of profound dementia with occasional ideas of persecution and auditory hallucinations. He was doubly incontinent, and noisy and troublesome at night. The physical state was characterized by generalized rigidity. He lay stiff and immobile, with his head off the pillow. There was no spontaneous speech and his replies were unintelligible. There was no lack of muscular strength but the patient seldom moved; passive manipulations revealed a definite hypertonus. A tendency towards the assumption of catatonic attitudes was noticeable. The tendon jerks were depressed and the plantar responses were equivocal in type.

Numerous other examples could be quoted from the literature, as the cases recorded by Cones [18], Reich, Martini and Isserlin [68], Pinéas [79] and [86], Stief [92] (Cases 1-5), and Urechia, Mihalescu and Elekes (Case 3). Many of Merzbach's [70] patients fall into this class, in particular his sixth and tenth cases.

Type 4.—Within this group are included cases in which physical signs of pyramidal disease, as bilateral extensor plantar responses and clonus, accompany those of pallidal origin. It is important that in contradistinction to the cases of so-called double hemiplegia and pseudo-bulbar palsy, dysphagia, dysarthria, and forced laughter and crying do not appear. This type of syndrome was familiar to Lhermitte under the title of "progressive pyramido-pallidal degeneration," and is now spoken of as "Lhermitte's disease." In his 1922 paper he gave an excellent example: A man aged 45 developed rigidity of the left arm and later of the left leg; his face was fixed and his trunk and extremities were intensely rigid. There was a relative akinesis with great slowness of movement. Later some dysarthria and speech difficulty appeared.

According to Lhermitte, the characteristics of the pyramido-pallidal syndrome are as follows:—

(1) Gradual onset and slow progression.

(2) A degree of hypertonus greater than in the ordinary pseudo-bulbar palsy, and rigidity combining the features of pyramidal with those of extrapyramidal disease.

(3) A Parkinsonian attitude of the hands.

(4) Slowness of movement, with a relative conservation of muscular force.

Lhermitte also includes pseudo-bulbar manifestations among the characteristic signs, but I do not consider these an essential feature of the syndrome.

As the disease progresses the pyramidal features may advance and overshadow the pallidal manifestations. The terminal stage is one of absolute helplessness. In a case recently seen in Professor Lhermitte's service at the Hôpital Villejuif there was a state of complete flexor quadriplegia, with contractures and emaciation; speech was impossible and swallowing was a matter of extreme difficulty. Consciousness was unimpaired and there was no emotivity.

Similar cases have been recorded by Lhermitte, Cornil and Quesnil, Buzzard and Barnes [12], and Lhermitte and McAlpine [61].

Type 5.—The conception of a clinical syndrome of vascular origin, combining the features of striate involvement with those of cerebellar disease, is by no means new. The so-called cerebellar types of pseudo-bulbar palsy illustrate this combination, and although but few exact pathological data are available, the clinical aspects have been long familiar.

One of the earliest cases described was by Raymond and Alquier [80]. Other instances have since been recorded by Garbini and Rossi [32], Lhermitte and Cuel [59], Sicard and Paraf [88], Crouzon, Dereux and Kensinger [20], Orzechowski [75] and Kleist (Case 7).

In 1927 and 1928 Freund and Rotter [29] and [30], in their papers on the extrapyramidal disturbances of movement in old age, described eight cases with autopsies. In four and possibly five (Nos. 1, 4, 5, 6 and ?7) lesions were found in the dentate nuclei, the olives and in the brachium conjunctivum, in addition to the typical vascular lesions in the striatum. Apparently these patients exhibited during life none of the manifestations ordinarily regarded as cerebellar, and they would clinically be relegated either to our first or third clinical group. The authors comment upon the remarkable pathological findings in their

fourth, fifth and sixth cases, and they regard them as examples of a peculiar type of strio-pallidal-dentate-rubral-peduncular system disease, hitherto undescribed.

The following case has been chosen to illustrate this particular type :—

H. B., male, aged 57, was admitted to the National Hospital (Dr. Collier), for pains and weakness in the legs which had been present for three years. His speech had gradually become indistinct. For about twelve months he had staggered while walking. Examination revealed a feeble man of subnormal intelligence. Articulation was slurred and there were recognizable traces of echolalia. Muscle tone was everywhere increased; the reflexes were exaggerated and the plantar responses doubtfully extensor in type. The motor power was good, but he was very inco-ordinate in his actions, and an intention tremor was demonstrable in both arms. There was nystagmus on lateral ocular deviation. The gait was propulsive and marked by very small steps. He was incontinent of urine and faeces. The blood-pressure was 220/130; the peripheral arteries were markedly sclerosed.

In a group apart we may consider those cases which are sometimes spoken of as "senile Vorsteifung," or Jakob's disease. The clinical picture resembles that of Type 3 in presenting a state of general rigidity and hypokinesis with dementia, but there are three main points of distinction: in the first place the mental symptoms may antedate the physical manifestations by a long period; secondly, the age of onset is later than in the majority of cases belonging to Type 3: thirdly, the evidences of arteriosclerosis may not be obvious and the blood-pressure is usually low. Few cases of this syndrome have been recorded, although its occurrence is well recognized in all institutions for the aged. Jakob, in his monograph on extra-pyramidal disease, gives a photograph of an illustrative case (Abb. 65) [42]. Although he gives no clinical particulars, the pathology of the syndrome is treated in detail.

A case recorded by Lemos in 1913 falls within this category: his patient—a 100-year-old negro—showed during the last few years of his life a bowed statuesque attitude; there was some tremor of the arms; he walked with small steps, and with some tendency towards propulsion. When turning he moved in one piece. His brain was afterwards studied by C. and O. Vogt.

The eighth case recorded by Freund and Rotter was regarded as one of Jakob's disease. Their patient, a female aged 77, became agitated and restless during the last five years of her life. She was slightly delirious at night. Three months before her death she became profoundly disorientated, and her agitation grew worse. Her gait was stiff: there was but little hypertonus beyond a slight resistance to passive manipulations of the right

leg. The reflexes were normal. Later, other symptoms appeared, such as echolalia, agnosia, motor apraxia and agraphia.

Syphilitic vascular Parkinsonism.—The possibility of a Parkinsonian syndrome due to pure vascular lesions of a sclerotic type is still further suggested by the paralysis agitans-like conditions secondary to syphilitic disease of the cerebral arteries. Such cases form a very well-known clinical entity which has been described for many years under various titles—tabes with paralysis agitans, syphilitic paralysis agitans, tromoparalysis tabetiformis, mesencephalitis syphilitica, "striatite syphilitique primitive." The symptomatology has been adequately discussed and the syndrome put upon a sound basis by the recent work of Kinnier Wilson and Cobb [104], and later still by Wohlfahrt [106]. Pathological study of this type of syndrome has been forthcoming in only a few instances. C. and O. Vogt found in the brain of a man with paralysis agitans and bilateral Argyll-Robertson pupils an "état lacunaire" in the striatum and pallidum. The papers of Urechia [94], Mella and Katz [69] and Lhermitte [56] have also contributed to our knowledge of its pathology.

Chapter III.—Symptomatology.

The clinical manifestations of the arteriosclerotic varieties of Parkinsonism resemble in no little degree those of idiopathic paralysis agitans; there are, however, some distinctive features in their symptomatology and also certain additional manifestations which are not found in the idiopathic cases. For this reason the clinical aspect will be discussed somewhat fully. It must be emphasized that individual patients show marked differences in the degree of affection, so that in the slighter cases there may be but few of the characteristic symptoms; on account of the comparatively rapid course of the disease, however, it is important to recognize the clinical manifestations of all stages.

The stance and attitude of these patients are so characteristic that an immediate diagnosis is often possible. There is a peculiar lack of mobility, so that the body moves as a whole without the play of the individual limbs or segments.

A mask-like fixity of the face is typical. It is incorrect, however, to describe the appearance as "expressionless," for the face in repose is full of emotional significance; as Hughlings Jackson has emphasized, a more accurate description would be to speak of the expression as fixed the lines of the face are carved into an image which does not change

with the passing mood. As a rule the expression is one of bewilderment, as portrayed by the elevated brows, the retracted lids and the gaping mouth. Nearly eighty years ago Rowland [84] commented upon the facial expression in cases of confirmed cerebral softening . . . "In old chronic cases that mixture of imbecility and astonishment which is so justly held to portray the disease is strongly impressed upon the features." The face immediately lights up upon appropriate stimuli, volitional or emotional. It is then apparent that there is no defect in the range of movement during the acts of showing the teeth, or screwing up the lids. Nor, in the early stages at least, is there any delay in the initiation of the movements or slowness in their execution. On the contrary, it is not rare to find an exaggerated play of facial movement during voluntary activity; in such a case the act of showing the teeth is executed with startling promptness, the lips are retracted to the widest possible extent, and may be accompanied by associated extraneous movements, with grimace-like effects. Emotional movements are also full in range and prompt in initiation and execution; in some cases, particularly when some degree of emotional instability occurs, there is a similar exaggerated facial activity. In other instances there may be an apparent dissociation between the individual facial movements, so that, for example, in the act of smiling, the lower half of the face alone moves, the upper portion remaining immobile—the so-called "adiadochokinèse de la mimique" (Steck).

It is noteworthy that there is usually no excessive sebaceous secretion, so that the facial greasiness of the ordinary Parkinsonian is not observed. Neither does one see the smoothing-out of the wrinkles which so often tends to produce an illusion of youth and belies the years of the Parkinsonian.

The head and neck are held upon the shoulders in an attitude of relative immobility; there is an absence of the quick lateral movements of the head seen in normal individuals; when the patient wishes to alter his direction or to look to one side, the head, neck and shoulders move in one piece and the movement is not broken down into its components. In early cases the stance is more erect than in the true Parkinsonian. When the patient walks, his neck and trunk are straight and his arms swing from the shoulders. The movements of the arms, however, are not entirely normal; they are often held rigidly away from the sides with the elbows partially flexed, so that the associated movement takes place at the shoulder-joints and not, as in the normal, at both shoulder and elbow.

When the patient is observed in bed, there is often a characteristic attitude of the head, the neck being slightly flexed, so that the occiput is held in the air unsupported by the pillow. Such an attitude—the "psychical pillow"—is not uncommon in many of the organic psychoses.

One of the chief clinical characteristics of the arteriosclerotic forms of Parkinsonism is seen in the gait. There is no excessive flexion of hip and knee as in paralysis agitans; at the knee-joint there is little or no flexion, and only the slightest bending at the hip; the steps are exceptionally short; one toe is usually advanced in front of the other no further than six inches, and often less. In the earlier stages the feet do not shuffle along the ground, but later they are no longer lifted. The trunk is not bent forward and the centre of gravity lies well above the base; festination and propulsion are, therefore, not seen. There is no widening of the base and no trace of inco-ordination. When the patient halts the stance is steady, without swaying or tendency to retropulsion. The characteristics of this gait are, therefore, those of the well-known "marche à petits pas," originally described by Dejerine, and associated by Marie and his school with the condition of progressive lacunar disintegration.

Sometimes a more flexed attitude of the trunk and limbs develops as the disease advances, while the onset of vertigo may influence the gait, causing the patient to sway while walking. Sometimes he is unable to remain in an erect attitude but sways backwards and falls. In such cases the muscles of the patient's foot contract forcibly in an attempt to steady the trunk, and the toes may be seen to become plantar-flexed in an effort to grasp the ground. Catola [13], who described this feature, spoke of the "claw-toes."

When the patient mounts or descends a flight of stairs the characteristic short-steppage elements are no longer apparent and the movements approximate more closely to the normal. If he goes up a slope the gait is less disturbed, but in descending an incline there is much difficulty and the steps become shorter and the progression is cautious and hesitant. Sometimes, through fatigue or nervouness, the patient, after taking a few steps, abandons his attempts at walking and seeks support, but with encouragement he is readily persuaded to continue. This modification of the ordinary "marche à petits pas" is sometimes known as "Petrén's gait."

Turning movements are carried out slowly and stiffly, the feet taking small steps. At first glance the head, neck and trunk seem to

move as a single unit, but on close examination it can be seen that the movement is decomposed into its constituent phases as in the normal individual, though each component movement is slow and minimal in degree. The arms are widely abducted as if the patient, anticipating a fall, were seeking support.

The patient moves from the erect to a sitting posture only with difficulty and with great slowness. In advanced stages this is impossible without assistance. A similar difficulty is experienced in getting up from a chair. At a late stage in the disease he may be quite unable to stand even with assistance.

Muscle tone.—It may be stated at the outset that there is usually some degree of hypertonus present, but it is uneven in distribution and variable in degree. This type of rigidity differs clinically from that associated with disease of the motor systems, and hence falls into the category neither of pyramidal nor of ordinary extrapyramidal rigidity. Moreover, there is an obvious relationship between the degree of hypertonus and the psychical activities of the patient, as evidenced by his power of attention, his ability to concentrate and his cerebration rate. A tendency towards the assumption of prolonged catatonic postures is an especial feature of this variety of hypertonus.

The rigidity is greater in the limbs than in the trunk, in the lower extremities than in the upper, and in the proximal parts of the limbs than in the distal. Thus, in the arms there is an obvious resistance to passive manipulation of the shoulder-joints, and a similar, though slighter, stiffness at the elbows. Passive extension of the fore-arm is more difficult than flexion and, indeed, in the severer cases, full elbow extension may be impossible. Usually there is little or no increase of tone at the wrists or in the phalanges, and the fingers can be bent back through a normal range by passive movement.

Though rigidity is slight or absent in the distal segments of the upper limb, the hands tend to assume abnormal postures which, however, can be passively corrected. Thus the fingers often remain extended at the interphalangeal joints, but are flexed upon the metacarpals, and the thumb is adducted. The terminal phalanges may actually show a hyperextension. Later the fingers and thumb become flexed and a "paw-like" attitude slowly results. The wrist is usually flexed and deviated to the ulnar side, the fore-arm pronated and the upper arm slightly abducted and internally rotated. It is important to realize that in the early stages these attitudes are readily altered by active or passive efforts, and appear to arise independently of contrac-

tures. Foerster [26] speaks of a specific flexing factor as responsible for the assumption of these characteristic postures.

A much greater degree of rigidity is always apparent in the legs. Both lower limbs are hypertonic but one leg may be more rigid than the other. Until the later stages, the attitude of the legs is that of extension, the feet lying in the equinus position. Adductor spasm is always present, and when one leg is picked up off the bed the opposite limb at once adducts to take up a position on the other side of the mid-line of the body. In bedridden patients, a characteristic attitude of the lower limbs may develop; one leg may be internally rotated and adducted, while the other limb is rotated outwards and abducted. The feet tend to become hollowed, though the high-grade deformities seen in severer states of pyramidal disease are rare.

Vigorous passive manipulation of the head on the neck and upon the shoulders usually betrays some increase of tonus, though the rigidity is rarely as great as in the legs. Similarly, passive movement of the trunk in all directions is resisted by some degree of hypertonus.

The nature of the rigidity differs from the more usual clinical varieties in several aspects: first, there is no approximation towards a a "clasp-knife" type of spasticity; in other words, the resistance encountered during passive flexion of a given joint is the same in all phases of the movement, and is no less at the end of the excursion than at the commencement. Neither do we encounter a cogwheel or punctuate type of hypertonus; the rigidity resembles rather that met with in paralysis agitans *sine agitatione*, in being "sticky" or "lead pipe" in character. It is constant in degree for all phases of a passive movement. Foerster speaks of the rigidity as being waxy. Secondly, the degree of rigidity does not lessen with repeated manipulation, unlike the spasticity of pyramidal disease, which tends to wear off with repeated forceful manipulations. Thirdly, the resistance is not the same in all movements of a given joint: thus it will be found harder to flex than to extend the knees, to straighten the elbow than to bend it. In this respect, the rigidity resembles that of pyramidal disease, and also (though to a minor degree) that of extrapyramidal affections. Fourthly, the rigidity is variable in degree. This is perhaps the most obvious feature and is one which gives the impression, on superficial or cursory examination, of a failure to relax on the part of the patient. To some extent, the amount of rigidity varies according to the force used in the passive manipulation; thus, at times vigorous movement of the limb seems to be opposed by an equally vigorous resistance, whilst

manipulations of less force appear to reveal a lesser degree of rigidity.[1] In this way there is a surface resemblance to hysterical hypertonus. The analogy must not be laboured, however, for other factors are traceable which influence the amount of rigidity. It is apparent to all observers that there is a great difficulty in obtaining satisfactory relaxation on the part of the patient. He usually behaves in one or two ways: either he is over-anxious to co-operate, and tries to assist the examiner by making active movements of a similar kind, or, more usually, he tends to adopt a resistive attitude and to tighten his musculature with a determination which is almost purposeful. To overcome this difficulty in relaxation and to eliminate any volitional factor, many devices may be found necessary. The patient's attention may be distracted by engaging him in conversation; it is a mistake to set him a mental calculation because, as Golla [36] has shown, abstract mental effort is attended by a slight increase in tone. The most successful measures require the intervention of a third party who will distract the patient's attention by talking to him or by examining some other part of the body. By one or other of these means it is usually possible to remove the personal element of error. But, when full relaxation has been obtained, a *marked degree of hypertonus still remains.* It may be said, therefore, that although the arteriosclerotic type of rigidity is characterized clinically by a difficulty in obtaining relaxation, it is, nevertheless, independent of the voluntary factor and still exists when all the elements of volition are removed.

The clinical manifestations of arteriosclerotic rigidity have been treated in detail by Kleist [49] under the term "Gegenhalten" (appropriately translated by Selling as "counterpull"). By "Gegenhalten" Kleist refers to the tonic contraction—manifest or latent—which can be brought out by passive movement of various parts of the body. It may be reactive (i.e., directed against passive manipulations) or spontaneous; it may be universal or local, and in the latter case it tends to be present in certain predilected parts, as the elevators of the jaw, the neck muscles, the trunk, the proximal limb segments and the adductors of the arms and hips.

Foerster lays emphasis on the existence in these cases of a phenomenon which he terms fixation-contraction ("Fixations-spannung"). If the points of insertion of a muscle are approximated to their fullest, and if

[1] Foerster, on the other hand, has described a directly opposite phenomenon; he states that in many cases the resistance can be overcome by gentle manipulation rather than by sudden or brusque movements.

the limb is held in that position for a moment before releasing it, the shortened muscle contracts forcibly and maintains the shortening for a time. Consequently, the limb remains in its new position and can only be extended by exerting a great deal of force. Although a similar phenomenon occurs in pyramidal disease, Foerster believes that fixation-contraction is stronger and more quickly elicited in states of arterio-sclerotic rigidity. It is immaterial, according to Foerster, whether the points of insertion of the muscle are approximated by activities of a volitional, automatic, or reflex nature, or even by electrical stimulation. In every case an identical fixation-contraction will result.

A certain degree of rigid fixity is present in the advanced stages of the disease, so that passive movement of one body segment becomes associated with a simultaneous and involuntary movement of another segment. Thus, passive dorsiflexion of the foot is accompanied by an immediate flexion of the knee and hip joints. If the patient's head is passively bent forwards on to the chest while he is lying supine, there is an associated flexion of the legs.

Palpation of the muscles themselves may reveal an abnormal hardness. This statement is especially true of the older patient. The distribution of this muscle hardness is not universal, however; when present it always occurs in the legs, while the muscles of the trunk and upper extremity are almost always of normal consistency to palpation. Associated with this increased firmness, one usually encounters an exaggerated mechanical irritability. The muscles may be bulky, but in the severer grades of cerebral arteriosclerosis the subject is often of spare build and meagre muscular development. In uncomplicated cases no fibrillation occurs, but it is actually not a rare finding, due possibly to concomitant spinal lesions of vascular origin. Electrical stimulation of the muscle produces a slow contraction which tends to persist for a little after the cessation of the stimulus; the relaxation is slow and gradual.

Attention has often been called to the striking visibility of the rigid musculature. Owing to the hardness of the muscular bellies and to their permanent state of increased tension, the muscular conformity of the limbs is frequently exaggerated. In the female subject, the contours may approximate to the masculine type. The tendinous insertions are tense and stand out clearly at the joints.

By employing various manœuvres it is possible to alter temporarily the degree of hypertonus. According to Foerster, the rigidity is increased by cold and is reduced by passive congestion, as by compression

of the limb with an Esmarch's bandage. I have not been able to confirm the latter observation, for I found no objective change in the degree of rigidity after or during the application of a tourniquet. Warmth exerts a very definite influence upon the muscle tonus; if the lower limbs are placed in a radiant heat bath for ten to twenty minutes an obvious decrease in the rigidity results. Immersion in a hot water bath has a similar effect. The decrease is purely temporary, however. The action of heat in reducing tone in arteriosclerotic rigidity is similar to its effect on spasticity due to pyramidal or extrapyramidal disease.

Liljestrand and Magnus [62] have shown that in decerebrate preparations the rigidity can be abolished locally by the intramuscular injection of novocain in doses too small to affect either the indirect faradic excitability or the reflex activities. Walshe has employed this method in his investigation of the rigidity in paralysis agitans. By de-afferenting a particular muscle with an injection of novocain near its motor point, the rigidity is temporarily abolished. An identical technique was employed by me in cases of arteriosclerotic rigidity. Novocain was injected into the deltoid muscles of patients in whom passive movements at the shoulder-joints revealed a high degree of rigidity. The injection resulted in a partial reduction of the hypertonus; although complete flaccidity was not produced, the diminution in hypertonus was unmistakable and persisted for about an hour.

There is little or no quantitative diminution in muscular power in cases of arteriosclerotic rigidity. Except in the later stages of the disease, the muscular force is commensurate with that of normal subjects of the same age and physique.

But while there is little or no paresis of the grosser movements of the larger muscle units, some subjective and objective defect in the execution of fine manipulative movements may exist and these become slow and awkward in execution: such acts as fastening buttons, tying and untying string, piano-playing, typewriting and card dealing may be clumsy or even impossible. The handwriting often betrays this weakness, and becomes angular, interrupted or irregular, and in cases with distal rigidity there is a micrographia comparable with that seen in idiopathic paralysis agitans.

Rapidly alternating movements are performed slowly and irregularly. The disturbance is different from that seen in cerebellar disease, for in the latter there is always an exaggerated play of extraneous muscles; in alternate supination-pronation of the forearm, for instance, the elbow is rotated in wide circles by associated abduction movements of the

upper arm. In arteriosclerotic rigidity there is much less defect of fixation, and associated movements in other parts of the limb do not occur to the same extent.

Bradykinesis, or slowness in the execution of voluntary movements, is one of the more characteristic signs. Thus, in the performance of the finger-nose tests the hand travels towards its goal with greater deliberation than normal. By ordinary clinical methods it is rare, however, to find any definite delay in the initiation or relaxation of a particular movement, except where cerebration is so retarded that the mental reaction time is prolonged. Foerster states that in the advanced stages there may be a very definite delay in the relaxation of a movement and the initiation of an antagonistic movement; the patient may show a little delay in reopening the closed fist after tightly clenching it. This observation has not tallied with my experience however.

Bradykinesis is not confined to those movements which one may regard as essentially voluntary. Slowness is also seen in acts which depend less on deliberate, volitional effort and which can be regarded more as "automatic." For example, if the patient is observed, without his knowledge, while he is eating or yawning, the movements are seen to be carried out with the same slowness.

Hall's accurate analysis [37] of bradykinesis has brought to light other points. He has confirmed, what has long been suspected on clinical grounds, that objective slowness of movement precedes the patient's knowledge of his disability. Patients with extreme bradykinesis show also a premature fatigue, which Hall terms "flagging." Although it is now agreed that bradykinesis is not necessarily dependent on rigidity, the two conditions are almost always combined. Moreover, an extreme degree of hypertonus increases the slowness of movement. On the other hand there is little or no relationship between muscular strength and bradykinesis.

The resemblance of the type of movement in arteriosclerotic rigidity to that in paralysis agitans is still further emphasized by the characteristic "poverty of movement" seen in each condition. This akinesis is most obvious when the patient is observed during the performance of some accustomed act, as reading or conversing; it is apparent that all expressional movement of the limbs and all play of gesture is reduced to the minimum, if not entirely absent. As Kinnier Wilson has pointed out in the case of the post-encephalitic syndrome, the patient never sits with the legs crossed or with the arms folded, does not fidget about in his seat, change his attitude or perform those numerous semi-purposeful

movements of the normal individual. He sits erect and immobile and employs as few extraneous movements as possible. Differences between the arteriosclerotic and other types of Parkinsonism are those of degree only, being less marked in the former condition.

Reference has already been made to the fact that these patients show a weakness of walking which is out of proportion to the relative strength of the individual movements of the limbs. Thus, whilst the patient is supine each component action can be executed with almost full power, and yet his gait is slow, short-stepping and feeble in the extreme. In other words, there is an apparent dissociation between the strength of volitional and of automatic movements. This dissociation has been emphasized by Lhermitte, who points out that such delicate and essentially volitional acts as writing may be carried out with accuracy, whilst the more elementary activities of walking, phonation and swallowing are grossly impaired. The type of case referred to by Lhermitte is, of course, severer than those I am describing and would conform particularly to those of Type 2.

The influence of the emotions upon these more automatic movements is frequently striking; under the influence of sudden fear or during an instinctive response to danger, the gait may lose its feeble and short-stepping characters and approximate to the normal. This paradoxical kinesis, which is, of course, a commonplace feature of the post-encephalitic varieties, is less well recognized and less marked in the arteriosclerotic types of Parkinsonism. By accurate ergographic measurements of the strength of Parkinsonians under mental stimuli, Hall has shown that an increase of output of rather more than 10 per cent. is possible. He suggests that some of the descriptions given of paradoxical kinesis are probably exaggerated.

It is necessary at this stage to examine briefly the state of the various movements of minor order attendant upon or forming part of the main movement-complex. Following the example of continental writers it had become customary to speak of these movements as diminished or absent in Parkinsonian states, to ascribe their abolition to disorder of the corpus striatum, and to attribute to the striatum the functions of "centre" for the regulation of associated movements. Kinnier Wilson [102], however, has proved each of these three views to be incorrect, and based upon inaccurate and insufficient observation. Wilson's conclusions have been fully confirmed by Young [107] in a series of post-encephalitic cases. In the present series of cases of arteriosclerotic Parkinsonians I have been able to support Wilson's conclusions.

The vague and inadequate term "associated movement" includes many varieties of movement, and therefore following Wilson's classification I shall divide them as follows:—

(1) Movement synergias. (Wilson rightly employs the simple term "movement" when referring to this type, but for the sake of clarity the earlier nomenclature will be adopted here.)

(2) Movements of co-operation.

(3) "Associated" movements properly speaking (or imitative synkinesiæ.)

(4) Movements of reaction and defence.

Within the first group Wilson has included those component activities enumerated by Beevor, which by their simultaneous or successive contraction go to form a complete "movement" (or synergic unit); the contraction of the extensors of the wrist and of the biceps during a forceful handgrasp is one example of the many normal movement synergias. In no instance of arteriosclerotic Parkinsonism which I have examined have I found an abolition of any of these component activities. Although slowly carried out, each constituent movement was present and of normal amplitude.

By the expression "movements of co-operation" Wilson understood "movements which are auxiliary to each other, also 'voluntary' movements preceding or accompaning these as the case may be." Foerster spoke of them as "reaction movements." One example will suffice: When a patient seated on a chair is required to stand he first of all brings his feet underneath his trunk so as to place them under his centre of gravity. No loss of this movement has been noted in any case examined in my series, though the movement may be slower in initiation and execution than in the normal subject. Much attention has been paid to a loss of swinging of the arms during walking as a mark of striatal disorder. In many of the cases of arteriosclerotic Parkinsonism, however, I have not found any abolition of these arm movements. Indeed, in some cases the movements are carried out in an exaggerated fashion, but the movements usually differ from the normal in that no excursion takes place at the elbow-joints.

By the term "associated movements" or imitative synkinesis one understands those symmetrical and synchronous movements of corresponding opposite limbs. The two chief predisposing factors for the occurrence of such movement are (*a*) rapidity or delicacy of movement and (*b*) forced effort. Hence the synkinesiæ are apt to appear either with fine manipulation of the fingers, or with vigorous actions such

as grasping. In executing the tests for dysdiadochokinesis, similar but mirror-opposite movements may often be seen in the contralateral limb. Synkinesiæ of this type may occur when the symptoms are bilateral and equal, as well as in those rarer cases in which the clinical manifestations are asymmetrical. In the latter case the synkinesiæ may appear in the less affected limb when the patient moves the more affected one—or vice versa. The imitation movements are feebler in force and amplitude than the primary movements; although "involuntary" in that they arise outside the subject's notice or volition, they are readily controlled when the attention is drawn to them.

Associated movements of this type are of course familiar in other pathological states, such as in pyramidal or cerebellar affections, in chorea, and in other states of Parkinsonism. Marie and Foix [65] indeed speak of a normal innate tendency towards imitation by one side of alternating movements of the other.

"Movements of reaction and defence" include those activities which result from definite noxious stimuli. Wilson has devised a series of chair-tilting tests to investigate the presence or absence of these movements. The manœuvres executed by the patient in the attempt to avoid a fall are noted. In not a few of the post-encephalitic Parkinsonians there is an apparent feebleness or absence of these movements. Thus Foerster remarked upon the indifference of such patients towards irritation from flies. Wilson was unable to find any constant absence of this phenomenon in post-encephalitic Parkinsonism, though there was a reduced response in some instances. In my series of cases of arteriosclerotic rigidity, in which these reactions were specifically investigated, no loss was encountered.

Analogous with these defence reactions are the so-called hyperalgesic reactions of Babinski and Jarkowski [45]. These authors found that noxious stimuli applied to the distal part of an affected limb in cases of hemiplegia may give rise to a series of reactions of varying complexity. There may be an abrupt and generalized withdrawal of the stimulated member; at the same time the upper extremity may move down toward the area stimulated, or in other cases be brought up to the head. Facial distortions suggestive of pain and exclamations of protest may also be present. The whole phenomenon, which is really only a natural response to unpleasant stimuli, is exaggerated in cases of pyramidal disease so as to amount to a veritable "réflexe de défense encéphalitique." In cases of Parkinsonism, however, Jarkowski found these "affectivo-motor reactions" (as he later called them) reduced or abolished.

One of the most characteristic clinical features of this variety of Parkinsonism is catatonia (or catalepsy). A tendency towards the assumption of fixed postures has been noted by many writers on the subject of cerebral arteriosclerosis. Foerster drew particular attention to it in his original monograph and likened it to a monosegmental catalepsy. Lhermitte and others describe how patients allow their limbs to remain immobile in unnatural antigravity postures . . . "as though they had forgotten them."

The presence of this catatonic tendency can be revealed by various devices. Thus if repeated passive movements of flexion and extension are made with the patient's upper limb and then support is abruptly withdrawn, the arm will remain for a time immobile. Again, if the patient's knee-joint is vigorously extended and flexed several times in succession and then suddenly released, the leg remains bent at the knee and ankle with the heel off the bed. Such an attitude may be maintained as long as half a minute. Sometimes if one raises one leg in order to investigate the tonus, the opposite leg is also raised and maintained for a moment or two in this unnatural pose. Foerster remarks that this catatonic tendency is especially marked if the attitude passively imposed is one of full degree, as for example full flexion of the elbow-joint, and that if the passive support is maintained for some little time before being released the catatonic tendency is usually pronounced.

In the severer degrees of arteriosclerotic Parkinsonism (as described under Types 2 and 3) catatonia is much more obvious and attitudes are maintained for longer periods. Moreover, the patient seems to adopt such postures as it were "spontaneously," without the intervention of passive manipulations (= the "spontaneous counterpull" of Kleist). Peculiar attitudes may be adopted: thus, one patient who belongs to Type 2 used to lie in bed with his left arm held stretched immobile immediately above his face, the limb lying at right angles to the long axis of the trunk, with the fingers fully extended and abducted.

This "spontaneous catatonia" must not be confused with the fixity of the patient in his characteristic flexor-attitude. Thus it would be incorrect to regard the bowed stance, the characteristic attitude of the upper limbs, or the "oreiller psychique" as evidences of a catatonic process. They are rather essential parts of the more universal "flexing factor" which Foerster holds responsible for the characteristic deformities and postures.

When the "flexing factor" preponderates, it may give rise to a

phenomenon which opposes and appears to be the direct antithesis of a catatonic process. Thus, if the typical flexion-supination attitude of the patient's fore-arm is passively overcome by extending the elbow-joint, one of two phenomena may occur: (1) If the catatonic process is the more obvious, the limb will remain in extension for an undue length of time, frequently in an actual antigravity position; (2) on the other hand, if the catatonic tendency is outweighed by the greater development of the "flexing factor," the fore-arm will slowly and involuntarily flex until it has resumed again its typical resting attitude. In this way the "flexing factor" and the catatonic tendency may appear as clinically opposite phenomena.

Speech.—Some defect of speech is usually present in all cases of arteriosclerotic Parkinsonism, whatever the clinical variety. In general terms it is one of articulating and not of propositionizing: all varieties of disordered enunciation are encountered up to total anarthria.

In the milder cases—as in Type 1—the changes may be so slight as to escape the superficial observer. The voice is hushed, the pitch being unchanged, and there is a lack of cadence so that the rising and falling inflections are wanting. Later, some defect in the pronunciation of the consonants appears, the labials and dentals suffering more than sibilants and gutterals. The defect becomes more obvious when the patient speaks rapidly, or employs unusually long or difficult words. The more advanced stages are marked by a simple exaggeration of these traits; the speech, which is now definitely dysarthric, is enunciated in a characteristic monotonous fashion.

Patients whose clinical picture conforms to Type 2 show the additional traits of pseudo-bulbar palsy. There is a superadded blowing or nasal intonation testifying to palatal weakness, and in certain instances a kind of verbal festination whereby the rate of speaking accelerates towards the end of the sentence. The rate of the speech as a whole is usually increased and the final syllables may be clipped in an abrupt manner. Lastly, there is a characteristic "explosiveness" so that the patient embarks upon a phrase in a sudden and unexpected way. During bouts of involuntary laughter or crying these disturbances of speech become greatly exaggerated. Indeed, in some mild cases, the speech may be almost normal during the inter-paroxysmal periods. In the emotional spells the dysarthria is, of course, greatly increased, owing to the lack of co-operation of the lips in speaking, and a "braying" element appears, which results from a stridulent expiration of air through taut vocal cords.

In the last clinical group, where cerebellar manifestations co-exist, the speech may show other characteristics; it may resemble that of disseminated sclerosis in being staccato or scanning, and the nasal element may be very pronounced.

Comparable with the hypokinesis of the motor system, a poverty of speech appears at a relatively later stage in cases of arteriosclerotic Parkinsonism. In severe cases this may amount to an actual mutism, which is especially seen in the third clinical type, where severe dementia accompanies the Parkinsonian syndrome. It is never absolute; the patient sits taciturn and immobile; he utters no spontaneous sound, and replies rarely and only to frequently repeated questions of the simplest order. The replies may be unintelligible, being grossly dysarthric and hushed. Moreover, the patient employs the minimum of words in his replies, which tend to be monosyllabic or telegrammatic in form.

Among the more interesting of the disorders of speech sometimes associated with the Parkinsonian syndrome must be included palilalia. This defect, which comprises the involuntary repetition several times over of the terminal word or phrase, is especially apt to be seen in Types 2 and 3. As pointed out elsewhere [19], palilalia frequently co-exists with some degree of mutism, as though the patient were unwilling to embark upon the act of speech.

The palate and pharynx: disorders of chewing and swallowing.—Defects in the functions of chewing and swallowing are uncommon in the arteriosclerotic types of Parkinsonism, except in conjunction with the pseudo-bulbar syndrome, but in cases conforming to Type 2 several important phenomena may be encountered.

Dysphagia is by no means uncommon, but differs from that occurring in the progressive bulbar palsies in being less constant and less severe. The difficulty, moreover, varies in degree from day to day in the same patient. In both disorders there may be dysphagia for certain types of foodstuff only—fluid or solids; in both, semi-solids are swallowed with least discomfort.

Difficulty of mastication is a frequent complaint in the pseudo-bulbar varieties of Parkinsonism, and results partly from weakness of the masseters and partly from disordered mobility of the tongue.

Nystagmoid movements of the soft palate, pharynx and vocal cords are not infrequent. As a rule they cause no symptoms and are discovered accidentally in the course of routine examination. The movement may be confined to either the palate, pharynx or larynx, but as a

rule all three structures participate in a rhythmic and synchronous movement. The involvement of the palate and pharynx is usually bilateral, while it is common for one vocal cord alone to be affected. The nystagmus occurs during rest and also during active movement of the part. The particular clinical group which is most apt to show these movements is Type 2, but they have also been seen in cases conforming to the fifth group.

The various reflex phenomena referable to the lips and tongue are of especial interest, but are apparently confined to the cases with "pseudo-bulbar" manifestations. These phenomena include the "buccal reflex" of Oppenheim (= "lip reflex" of Thomson) — the "hard-palate reflex" of Henneberg and the orbicularis reflex. They comprise the production of pouting, sucking and chewing movements ("Ansaugen") upon appropriate stimuli.

Reflexes.—The state of the superficial and deep reflexes varies a great deal, depending not only upon the clinical type of Parkinsonian syndrome, but also upon the presence of various extraneous factors. Thus, in addition to the co-existence of pyramidal affection or of cerebellar disease, one must take into consideration the influence of such all-important factors as age, decubitus, presence of contractures, arthritis deformans and muscular wasting. By reason of their frequency it will be advantageous to consider them at the outset.

Although all patients with arteriosclerotic Parkinsonism do not necessarily fall into the category of senescence, nevertheless advanced age commonly complicates the clinical picture. Its influence upon the state of the reflexes is proved, but the actual nature of such changes is a subject upon which no exact information is available. There is certainly, however, a frequent depression in the activity of the deep reflexes. The effect of old age upon the pupillary responses, and upon the rectal, vesical and genital reflexes will not be considered. A diminution and later abolition of the abdominal response is, of course, well known. Absence of the Achilles jerk with conservation of the knee and arm reflexes, is by no means an uncommon finding in healthy old age. It is doubtful whether a Babinski type of response is ever seen in cases of normal senescence, although occasionally said to occur.

In bedridden patients with cerebral arteriosclerosis the tendon reflexes become further altered by the development of contractures. A permanent attitude of flexion results and it may be quite impossible to elicit patellar or ankle jerks. Arthritic changes, particularly in the upper extremity, produce a similar difficulty in testing the reflexes.

In the few cases in which the influence of advanced age, of contractures and joint changes is non-existent, the tendon-jerks are active, but the typical motor response is slow and gradual in attaining its summit and the return to the resting posture is prolonged. Clonic responses are not usually obtained. The abdominal responses may be elicited, but they tire readily, so that after three or four successive stimuli no contraction results.

In uncomplicated cases the plantar responses are of the flexor type. I have not succeeded in changing the character of the reflex by altering the posture of the head or neck (Walshe [101]). Rosenfeld's method [83] of changing the character of the plantar response by means of hyoscine has not been tried in this series.

In cases in which a pyramidal affection exists in association with the pallidal disease, there is a change in the character of the tendon-jerks. The delayed contraction and gradual relaxation are less noticeable and a clonic element is superimposed. This latter may only be revealed by graphic methods. The superficial abdominal responses are abolished and the plantar reflexes are extensor in type. Sometimes, when the pyramidal disorder is presumably slight in degree, the plantar response may be extensor in type when the stimulus is applied to the outer side of the sole, and flexor when the inner side is stimulated.

Another type of variability in the plantar response has been noted in cerebral arteriosclerosis by Buzzard and Barnes. In their patient plantar stimulation evoked an extensor response when the leg was extended, but the reflex changed to the flexor type when the limb was flexed. They applied the term "pyramidal equilibrium" to this phenomenon.

Hyperkinetic manifestations.—Besides the hypokinetic-hypertonic manifestations which, as we have seen, form the background of this syndrome, other symptoms of a hyperkinetic nature are occasionally encountered. These are of the utmost diversity and vary in complexity from involuntary movements of a simple repetitive nature to complicated psychomotor activities of an almost purposeful type. Thus at one pole we have simple tremor or choreo-athetosis representing a hyperkinesis which is purely involuntary and almost beyond the control of volition: at the other extreme lie the parakinesias, expressive movements, motor stereotypy, the echopraxic and palipraxic phenomena, movements of sucking, tasting and smacking of lips ("Ansaugen"), forced grasping and groping, clutching movements initiated by visual stimuli, akathisia, movements of rubbing and stroking and so forth.

Many of these activities have been studied by the German school, particularly by Kleist [47] and [48].

Hyperkinetic manifestations are on the whole uncommon in arteriosclerotic Parkinsonian states: the absence of tremor is indeed a point of differential diagnostic importance. When the more complex psychomotor signs occur there is usually a severe co-existing degree of intellectual enfeeblement. This does not hold true for the simpler types of involuntary movement of tremor or chorea. In diffuse cerebrovascular disease when akinetic phenomena are prominent there are as a rule few, if any, evidences of hyperkinesis, but exceptions occur. Thus in the second case of Stief, Kleist's Case 1, and Freund and Rotter's first patient, tremor of hands, head or jaw, was associated with arteriosclerotic Parkinsonism. Sicard and Paraf's patient exhibited choreo-athetotic movements: movements of grasping and groping ("Zwangs- und Nachgreifen, optisches Kurzschlusshalten, Festhalten") were described in association with a hypokinetic-hypertonic syndrome by Schuster and Pinéas and by Kleist (Cases 1 and 7, of 1927). The behaviour of these patients closely resembled that of some of the patients with frontal tumour described by Adie and Critchley [1].

Involuntary movements of the palate, pharynx and vocal cords were seen in the cases recorded by Crouzon, Dereux and Kensinger, Signorelli, Lhermitte and Cuel, and Lhermitte and McAlpine. Lastly, among the miscellaneous involuntary movements of complicated order may be mentioned Stief's fourth case, the first and sixth cases of Kleist's (1922 paper) and Noethe's patient. One patient in my series exhibited many psychomotor activities in the form of plucking at his nightdress, fingering the coat and stethoscope of the examiner, touching, rubbing and stroking.

Kleist's first patient (1922 and 1927 papers) showed explosive mimic movements and sucking, as well as forced grasping. In the right hand there were, in addition, movements of pill-rolling, rubbing, grasping and touching. In Case 6, parakinesis and palipraxia were present.

Noethe's patient showed with the left hand movements of striking the head, clutching the hair, grasping the genitalia, shaking hands, pulling at the bedclothes, forced grasping and echopraxia.

Stief's fourth patient performed complicated movements of packing objects in bed; and at a later stage, when grossly demented, she would slowly transfer to the mouth any object placed in the hand.

The psychological aspect.—Psychical changes are both frequent and important in the arteriosclerotic varieties of Parkinsonism. In some instances mental change appears very early and may indeed antedate

the appearance of physical disorder ; in such cases the psychical manifestations tend to occupy the foreground of the picture. Other cases show little or no mental change until the terminal phase of the disease. Cases which I have relegated to the second type are especially prone to be characterized by psychical defect, but none of the other groups is exempt from similar change.

In the milder cases the onset of the intellectual impairment may for a long time escape notice, and such changes as may be present are often ascribed to senility. The severer grades are usually regarded as examples of senile or arteriosclerotic dementia.

The main psychological features indicate a gradual process of cerebral dissolution : in short, they comprise a global dementia, which may be variable in degree, together with some change in affectivity. The earliest signs usually appear insidiously, although an acute onset following a stroke or an illness does not argue against the diagnosis. Among the early symptoms is a falling off in the patient's intellectual capacity ; he may still be able to cope with the ordinary routine of his occupation, but any fresh or unusual demand upon his intellect fails to evoke the normal ready response. This failure of mental elasticity causes the patient to feel jaded and harassed when faced with problems lying outside his usual experience. An anxiety state not infrequently results and many patients seek advice and are treated as "neurasthenic." These delicate criteria of dissolution may not be apparent in the less cultivated type of individual ; in the words of Hughlings Jackson [40], "much depends upon the type of brain he had before his illness."

Later, the patient may show an unwillingness to cope with novel situations or to embark upon unwonted enterprises ; he tends to "fall back upon himself" and to be inattentive to external concepts and stimuli. He then appears forgetful of the trivial events of the day, and complains of defective memory. There is no failure, however, in recalling the remote past, and in later stages we find the "anecdotage" and conservatisms of senility.

Parallel with this intellectual impairment, a gradual limitation of the field of interest is often apparent. The patient becomes self-centred and frequently selfish, and the troubles of his friends and relatives leave him singularly unmoved. But within this narrowed sphere there is an instability in the emotional tone and a corresponding lack of expression-control. Tears and laughter are readily evoked, frequently without corresponding affective concomitants.

Variability in the degree of mental change is often striking. Many

of these patients have periods of clarity which alternate with periods of clouded consciousness. Under treatment, or after admission to hospital, the symptoms tend to improve in a striking way. Hughlings Jackson [40], speaking of the mental symptoms of softening of the brain, distinguishes carefully between the active or positive manifestations due to the removal of inhibitory control and the negative ones which result from the loss of substance of part of the functioning brain. The latter type of change, he states, may slowly develop weeks, or even months, after an acute vascular crisis. A consideration of the individual symptoms as occurring in a severe or long-standing case may be shortly considered.

Disturbance of the centripetal functions is present in all severe cases, so that the patient's perception is defective and delayed; in severe cases there is no link whatever between the patient and his environment. Illusions, or perverted comprehension of precepts, are not common. Hallucinations may occur, but are rarely systematized or vivid.

Ideation and the power of abstract thinking is, of course, completely lost in the severest stages, but an assessment of the patient's ability is much impaired by difficulties in co-operation; defects in self-expression and the delayed perception may give rise to an erroneous and inadequate idea as to the state of mentation.

Association processes are characteristically retarded in the arteriosclerotic, and the number of available concepts is reduced. Processes of calculation and of expressing a coherent opinion upon an abstract subject are impossible. The patient passes with difficulty from one idea to another, and the first concept, once grasped, tends to occupy consciousness to the exclusion of fresh incoming ideas (ideational inertia: perseveration). A similar lack of mental agility is also seen in some cases of post-encephalitic Parkinsonism, and to this Claude has applied the term bradyphrenia, or "mental viscosity." Delusions or erroneous ideation may occur and take many bizarre forms. Among the more usual varieties are nihilistic, hypochondriacal, and micromanic delusions.

Disorders of memory are among the earliest and most characteristic of the psychical aberrations. A defective impressibility is a most obvious feature, so that the memory for recent events always suffers much more than that of the distant past. Sometimes the memory of familiar surroundings may be so impaired that the patient loses himself in his own house and is unable to find his way about the neighbourhood. Confabulation is not a feature of this type of disorder. Bleuler has called attention to the presence in the senile of cryptomnesia, whereby

the patient, having at first rejected a new idea, finally assimilates it and then publishes it and passes it on as original—perhaps even to the very person whence it was obtained. Disorientation as to time, place and person is almost constant.

Clouding of consciousness, either permanent or episodic, may occur in the late phases. At night-time there is frequently some degree of delirious excitement which contrasts strangely with the patient's diurnal impassivity.

Changes in affectivity are frequent; in the earlier stages, particularly in cases belonging to Type 3, there is a marked emotional incontinence with spontaneous weeping and laughter. It is doubtful, however, whether these emotional displays are in any way a true representation of the actual feeling tone. Certainly in the later stages there appears to exist an apathy. When there is a constant departure from the normal feeling tone, the usual affect is one of depression rather than of exaltation.

The power of attention suffers in most instances—so that there is a difficulty in fixing the patient's mind on a particular theme. Once the attention is aroused, however, a marked prolongation occurs, and the mind is with difficulty directed towards a fresh idea.

Suggestibility is usually defective; in some cases a negativistic trend is present, so that suggestion evokes a contrary response. Alterations in personality, in the nature of transformations, are not usual in this type of patient.

The diagnosis from other senile and presenile psychoses is not readily made on purely psychiatric grounds. Although there is usually little or no difficulty in distinguishing a pure case of senile dementia from one of arteriosclerotic dementia, nevertheless in cases of arteriosclerotic Parkinsonism the mental symptoms may resemble either type. Thus one patient may show mental symptoms conforming to the arteriopathic order, and another to those of the senile type. Characteristic hypertonic-hypokinetic signs usually differentiate these cases from the other degenerative psychoses, such as Pick's disease, Alzheimer's disease and presbyophrenia. Furthermore, the pathological restlessness seen in the early stages of Pick's disease and presbyophrenia rarely occurs in the arteriosclerotic Parkinsonian.

Onset and course.—In the majority of cases the onset of the Parkinsonism is insidious and the progress steady and gradual. There is no history obtainable of any preliminary stroke. The course of the malady therefore resembles that of the idiopathic variety, but differs in being more rapid.

A smaller group of patients with arteriosclerotic Parkinsonism date their symptoms from an abrupt onset, which is usually of the nature of a mild apoplectic stroke. The progress of the disease is then characterized by a series of mild seizures, mostly of temporary character, but followed by a slight though definite increase in the basic disability. Marie, Ferrand and others have stressed this latter type of progression and have associated it with the pathological conception of progressive lacunar disintegration. Each attack is transient and is not attended by loss of consciousness; the paralysis is usually slight in degree and frequently monoplegic in distribution. Ferrand and his co-workers were mainly interested in the phenomenology of these acute exacerbations; it is the resultant chronic condition which we are at present considering under the category of arteriosclerotic Parkinsonism.

There is a third and still rarer mode of onset in these hypokinetic-hypertonic syndromes of arteriosclerotic origin: thus a unilateral Parkinsonism may follow a stroke. In such cases a hemiplegic distribution of rigidity, with little or no paralysis, no tremor, and no reflex evidence of pyramidal disease constitutes the clinical picture. Amongst cases of this type, recorded in the literature, are those of Bechterew [5] (who employed the term "hemitonia apoplectica"), Pfeiffer [77], Loewy, Mingazzini (whose case was peculiar, in that the clinical signs were on the same side as the pathological lesion), and Boettiger [6], who spoke of "hemi-hypertonia apoplectica" or "extracapsular hemiplegia."

The termination of the malady is always fatal, though the exact mode of death is variable. In some cases the patient becomes bedridden and incontinent with the legs completely paralysed in extreme flexion; difficulty in swallowing appears and he can no longer feed himself; articulatory defects render the patient unintelligible: consciousness is clouded and intellectual enfeeblement is profound. The ultimate phase is that of the "démence paraplégique" described by Deny and Lhermitte. Death usually results from broncho-pneumonia.

Such is the characteristic termination in the decrescent or senile type of arteriopath. In younger patients, in whom there is usually an increased blood-pressure, death may be sudden. In such large vascular lesions of a focal nature are common and the patient succumbs to a severe cerebral hæmorrhage or softening.

Differential Diagnosis.

The diagnosis of cerebral arteriosclerosis is usually easy and cases of arteriosclerotic Parkinsonism are often recognized at sight. The

differences between arteriosclerotic Parkinsonism and other syndromes of cerebral vascular disease are those of degree rather than of quality. As previously emphasized, the pseudo-bulbar, the lacunaire and the arteriosclerotic dement frequently show in some degree the features of Parkinsonism, and a too sweeping classification of cerebral arteriosclerosis is neither possible nor desirable. Most difficulty lies in the differentiation from idiopathic paralysis agitans. As previously stated, it is doubtful to what extent the two conditions are actually separable; cases exist which are difficult to place in their proper grouping and these probably represent transition types. Usually, however, the two conditions are clinically distinguishable.

The onset of the symptoms may be different in the two cases. In the idiopathic variety the disease starts insidiously; a similar mode of onset may occur in the arteriosclerotic, but in a certain number the symptoms date from an acute apoplectiform attack. Secondly, the course may vary in the two diseases. In true paralysis agitans the advance is slow but steady. In arteriosclerotic Parkinsonism the advance is usually more rapid, or the disability increases by a series of step-like progressions, each exacerbation corresponding to a mild seizure.

The clinical manifestations are not quite identical. Thus a monoplegic or unilateral distribution of symptoms is rare in the arteriopathic varieties though common in paralysis agitans. In both types the facial expression is fixed, but in most of the vascular cases there is little or no smoothing out of the wrinkles and less facial greasiness. Typical pill-rolling tremor is almost always absent from the arteriopathic cases, though a "senile" type of tremor may be seen in the head, jaw or hands of the decrescent cases. The character of the rigidity is very similar in the two conditions, but the "cogwheel" phenomenon is rarely obtained in the arteriopath. Some authorities have been impressed by a greater firmness of the muscles on palpation in arteriosclerosis, but my experience does not altogether support this view, except in some of the older and bedridden patients. Jakob and others believe the muscles and tendons stand out more prominently in the symptomatic types. In the late stages the arteriopath probably shows more contracture and joint change than the true Parkinsonian. One of the most important points of differentiation is catatonia, which is rarely seen in true paralysis agitans. Severe symptoms referable to the bulbar mechanisms (dysphagia, dysarthria, sialorrhœa) suggest an arteriosclerotic basis to the malady. In most cases of arteriosclerotic

Parkinsonism the gait differs in certain minor particulars from that of true paralysis agitans. For example, the arteriopath almost always swings his arms, though in a stiff and automaton-like manner, and festination and propulsion are less obvious.

Psychical changes are important in differentiating the two types. Mental enfeeblement is an uncommon symptom of paralysis agitans and never appears until the late stages. In the arteriopath mental changes are, of course, very common: they are severer in degree and earlier in their appearance. The presence of emotional instability, with facile laughter and tears, is strongly suggestive of a vascular basis. Incontinence of urine and fæces rarely occurs in genuine paralysis agitans; indeed Gowers stated he had never met this symptom, while defective sphincter control is frequent in the arteriosclerotic forms.

In distinguishing between the two types, evidences of peripheral or retinal arteriosclerosis must be sought for. A negative finding does not, of course, exclude the cases of senile rigidity nor altogether the arteriosclerotic types; on the other hand, the demonstration of definite arterial disease in the periphery is suggestive of a vascular origin.

The presence of other focal manifestations (cerebellar or pyramidal signs, aphasia or apraxia, palilalia, choreiform or other involuntary movements not seen in paralysis agitans) suggests an arterial origin.

Lastly, the age factor is often helpful. Idiopathic paralysis agitans is a "disease of the degenerative period of life, but not of extreme senility" (Gowers). In the majority of cases, the symptoms arise in the sixth decade: the average age of onset was 52 in Gowers' series, while it was rare for symptoms to appear after the age of 65. In the arteriopathic cases the age of onset varies according to the type of arterial disease; many of the cases associated with hypertension and arterial changes of moderate degree start at a comparatively early age; many of them become affected between the ages of 40 and 50. With the cases of decrescent vascular degeneration, however, in which the blood-pressure is often low, the age incidence is much later and as a rule occurs at a later stage than paralysis agitans. An onset after the age of 65 is not uncommon in such cases, many of which belong to the clinical sub-type of senile rigidity. In short, symptoms of Parkinsonism commencing either early or very late (before 45 or after 70) are more likely to belong to the arteriosclerotic category.

Apart from other syndromes of cerebro-vascular disease there are but few disorders which bear any resemblance to arteriosclerotic Parkinsonism. Cases of post-encephalitic Parkinsonism occurring in middle or

advanced life may cause confusion, but can be distinguished by the presence of ocular signs, by a greater degree of greasiness of the skin, and by different psychological concomitants, quite apart from a history of acute encephalitis.

Cases of mesencephalitis syphilitica are distinguished by the presence of additional characteristic signs, such as pupillary alterations, hypalgesic areas, defective postural sensibility and abolition of the tendon reflexes. A history of venereal infection and positive serological tests confirm the diagnosis. In these cases, too, the evidence of a peripheral arteriosclerosis may be wanting.

Reference has already been made to those states of pseudo-Parkinsonism which may accompany ankylosing spondylitis or arthritis deformans. Except in cases where true paralysis agitans co-exists with severe joint changes, there should be no real difficulty in distinguishing them.

Some difficulty may be anticipated in separating the cerebello-pallidal type of arteriosclerotic Parkinsonism from other cerebellar syndromes of the aged, in particular olivo-ponto-cerebellar atrophy (Dejerine and Thomas), olivo-rubro-cerebellar atrophy (Lejonne and Lhermitte), delayed cortical atrophy (Marie, Foix, Alajouanine, etc.) and the various transitional forms (Ley). These disorders are, as far as we know at present, associated with a senile process and bear no direct ætiological relationship to cerebro-vascular disease: hence the presence of peripheral or retinal arteriosclerosis will suggest a cerebello-pallidal syndrome. A sudden or apoplectiform onset, or a step-like progression in a downhill direction, suggests cerebral arteriosclerosis. The co-existence of other focal brain manifestations is not to be expected in the senile cerebellar syndromes. The presence of well-defined extrapyramidal signs (bradykinesis, mask-like face) are points in favour of cerebral arteriosclerosis. Lastly, the true senile cerebellar syndromes are not, as a rule, associated with mental change. In the majority of cases the state of the muscle tonus is a valuable diagnostic point, for a normal or diminished tone occurs in the senile atrophies, though in the terminal phase rigidity may be present (Ley [51]).

Differentiation has also to be made, as Lhermitte has shown, from those cases of senile paraplegia due to purely muscular changes. The main distinguishing feature of senile myosclerosis is a high-grade generalized muscular wasting with myoidema; the course is slower and there is a relatively long interval between the affection of the legs and implication of the trunk, neck and arms. Frequently passive

manipulations of the affected limbs are impossible, and attempts at so doing elicit pain. In addition, there are two symptoms of arteriosclerotic rigidity which are rare in senile myosclerosis, namely catatonia and mental change.

Chapter IV.—Morbid Physiology.

The nature of "arteriosclerotic rigidity."—A certain amount of doubt exists as to whether a single pathogenic agent is responsible for the various forms of rigidity met in arteriosclerosis. In a large proportion of the cases the hypertonus cannot be due to pyramidal disease, and even when this is present it obviously cannot account for the whole of the rigidity.

The "plastic" character of the hypertonus, the bradykinesis, the poverty of spontaneous movement, the attitude, facies, stance and gait of the patient suggest a close analogy with the amyostatic syndrome of extrapyramidal disease. It has been customary, therefore, to attribute these symptoms to disorder of the corpus striatum, and of the pallidum in particular. Hence the syndrome of arteriosclerotic rigidity has been associated with the hypertonus of idiopathic paralysis agitans.

Before accepting such an opinion unconditionally, it is advisable to broaden our observation of the clinical phenomena and interpretations thereof rather than to focus the whole attention upon the pallidum. Closer examination of the character of the rigidity and the factors influencing its intensity, coupled with an appreciation of the psychological aspect of the patient, will reveal other features which do not form an essential part of the true Parkinsonian syndrome.

In the first place, the hypertonus appears to be more under the influence of psychological factors in the arteriopath than in the true Parkinsonian. Thus, the degree of rigidity varies with the amount of force used in passive manipulation. Again, by distracting the patient's attention, the degree of rigidity is lessened, although not removed. In some patients these factors are so obvious that the rigidity may lightly be attributed to an inability to relax. But when by appropriate measures the whole of the psychological factor is eliminated there is still an obvious residuum of increased tonus. Foerster has shown that this rigidity is demonstrable even during sleep. On the other hand, by employing those devices which remove the reflex component of the rigidity (i.e., by novocain de-afferentation) an obvious reduction occurs in the degree of hypertonus.

Nor is it wise or even justifiable to disregard entirely the obvious

"difficulty in relaxing" which these arteriopathic patients show. This inability to relax, so constant and so potent a factor in this disorder, is seen in few other clinical conditions with the same frequency or intensity. It may well be compared with the rigidity occurring in cases of dementia præcox, in which the rigidity is the physical reflection of the mental state of negativism. A similar state of mental resistance does not occur in cerebral arteriosclerosis to the same extent, although it cannot be said to be entirely negligible. Kleist indeed regards a state of psychomotor negativism as all-important in the production of counter-pull. Psychological factors of even greater prominence in the cerebral arteriopath are a defective accessibility and an impaired appreciation of the impressions received. This intellectual defect is mirrored in the physical condition by an impaired ability to grasp the wishes of the examiner, or to assist him by the relaxation of the muscles. Passive manipulation of the extremity, therefore, produces an automatic and almost "reflex" tightening of the muscles as if in opposition.

Inability to pass readily from one concept to another shows itself by a failure to grasp quickly what is required. This ideational inertia is reflected in the physical state by a tendency towards motor perseveration, so that successive commands may evoke identical responses. To some extent the hypertonus may be the expression of a perseveration whereby rapidly alternating passive movements, as of flexion and extension of a limb, tend to be resisted. Two chief clinical phenomena illustrate this point: first, if the limb is rapidly moved in a direction of alternate extension and flexion, and then abruptly released, the patient may of his own accord continue to make feeble flexion-extension movements simulating those carried out by the physician. These palipraxic "after-movements" persist for only a short time. The second illustration lies in the assumption of catatonic postures, a feature which will be discussed later.

When evaluating the various factors in arteriosclerotic rigidity, it is necessary also to investigate the peripheral mechanisms. Changes of a senile or trophic character in the joints, tendons, or muscles are frequent and important factors. The presence of a deforming arthritis in the joints of the limbs is of itself apt to produce, by a process of partial ankylosis, a spurious increase of tone in the affected extremity. This pseudo-rigidity, combined as it often is with a poverty of spontaneous movement and slowness in execution, may simulate the hypertonic-hypokinetic syndrome of paralysis agitans. Indeed, through the writings of Brissaud, Delachet, Sicard [87], Lhermitte, Steck [91] and

others, the French have been long familiar with the clinical conception of a "syndrome parkinsonienne à forme arthritique" or the "maladie de Charcot-Landré-Beauvais." The stance and bowed attitude of the Parkinsonian, and even the impassive face, is closely simulated in the aged by conditions of cervico-dorsal kyphosis, with ankylosis of the occipito-atlanto-axis articulations, a clinical commonplace in institutions for the aged.

Contractures appear early in senile and arteriosclerotic rigidity, and advance apace as soon as the patient becomes bedridden. Typical deformities appear in the hands; the flexed attitude of the legs becomes extreme, so that passive extension is quite impossible, and the tendon reflexes become difficult to elicit.

The causation of early contracture in arteriosclerosis is obscure, but is usually attributed to implication of the meninges or ventricles (Gaussel [33]. In cases of multiple vascular lesions, however, a type of contracture may appear which is spoken of as "pseudo-précoce," that is to say, a slight and transient stroke is followed almost immediately by the development of contractures of a "late" type. Bard [4] has suggested that in such cases the contracture is really an expression of diffuse or multiple lesions; the stroke which appears to be responsible is not the sole agent, for other and slighter seizures have occurred previously; hence the contracture is a "late" one if dated from these original and often negligible attacks. Such an hypothesis may be applicable to the severe and early development of contracture in cases of arteriosclerotic Parkinsonism.

Other severer and more permanent shortening processes may occur in the tendons around the joints. These "retractures," as they may be called, do not disappear under even the deepest anæsthesia, and after death tenotomies may be necessary to straighten the limbs.

Fibrotic changes in the muscles themselves still further augment the rigidity. Lhermitte, both alone [52 and 55], and in collaboration with Lejonne [50], has described under the title "Myosclérite rétractile progressive," or "Myopathie sénile et primitive," the clinical and pathological aspects of this complicating factor which develops with such rapidity in the bedridden patient. The aged are particularly susceptible. Changes of this character located within the muscles contribute to the feeling of hardness on palpation. Moreover, the intrinsic changes in the muscle assist in the so-called "formgebenden" rigidity whereby tendons and muscles stand out prominently in contour. There is always a great diminution in the bulk of the muscle, and the mechanical excitability

is increased. The muscles are tender on palpation and attempts at passive manipulation are painful. No changes occur in the reflexes; sensibility is intact; there is a slight diminution in electrical excitability but no reaction of degeneration. It is remarkable that so important a clinical observation as the existence of a senile form of myosclerosis should escape comment, although the subject has been reopened in more recent years by Funet [31].

In cases of partial or intermittent ischæmia of the extremities from disease of the peripheral vessels, there also occurs rigidity or cramp of a temporary nature. Thus, in cases of intermittent claudication the affected muscles go into a state of spasm coinciding with the period of least arterial supply. To a lesser degree the same phenomenon may be seen in Raynaud's disease and in acroparæsthesia: similar states of peripheral arterial disease are present in many of the cerebral arteriopaths, and it is highly probable that spasticity of peripheral origin contributes to the total rigidity. Such a conception would explain in part the marked influence of cold in increasing the rigidity.

Finally, account must be taken of the possible existence of changes in the peripheral nerves. Although comparatively little attention has been paid to the subject, the evidence of Schlesinger [85], Franceschi [28] and others, demonstrates that a peripheral neuritis of an arteriosclerotic basis does occur. In certain instances of diffuse cerebro-vascular disease, therefore, it is possible that changes in the peripheral nerves contribute to the hypokinesis, as well as to the formation of contractures and intramuscular fibrosis.

When rigidity of a pyramidal order is demonstrable there will appear characteristic tendon responses, knee and ankle clonus, and Babinski's phenomena. A true defence reflex may be obtainable. It is to be noted, however, that all the reflex signs of pyramidal disease cannot always be demonstrated, and sometimes ankle and knee clonus may be obtained whilst the plantar reflexes remain flexor. Conversely, extensor plantar responses may exist without any clonus being obtainable.

Buzzard and Barnes have described under the term "pyramidal equilibrium" a condition in which the functional integrity of the pyramidal tract seems to waver in the balance. It may be advisable to recall at this point the work of Walshe [100], and also Marinesco and Nicolesco [67], who found, after the injection of hyoscine in cases of idiopathic paralysis agitans, that the plantar responses temporarily became extensor in type. Walshe discussed the possibility of a clinically latent disturbance of pyramidal function being present in apparently pure examples of paralysis agitans.

We are led, therefore, to a wider conception of the pathogeny of the rigidity syndromes in cerebral arteriosclerosis. It is no longer justifiable to attribute the hypertonus wholly to pallidal disease, in fact, it seems that lesions at all levels of the central nervous system, and even of some extraneural mechanisms, may contribute. And we cannot disregard the psychological factors, as defective co-operation and even active resistance. The pyramidal motor system certainly contributes to the rigidity in a proportion of cases. Lastly, structural changes in the joints, tendons, muscles, and peripheral blood-vessels may play an important rôle.

Reference has already been made to the extreme difficulty with which voluntary resistance and failure to relax are overcome in the arteriopath. In some of the more demented patients it is possible that this factor is insurmountable. Wilson has suggested that even in those in whom an apparently complete relaxation has been effected there still remains an element of psychomotor resistance over which the patient has no voluntary control. In such cases one is struck by a similarity with the phenomena of apraxia and the possibility of an unconscious apraxic type of rigidity must be borne in mind.

The nature of catatonia.—The frequency with which attitudes passively imposed are maintained by the patient is a striking feature of the cerebral arteriopath. This manifestation is especially common in all Parkinsonian syndromes associated with arteriosclerosis, and occurs in all the types described.

Much confusion has arisen with regard to terminology. The word "catatonia" has been employed throughout this paper to describe this phenomenon, in spite of possible confusion with that type of dementia præcox named "katatonia" by Kuhlbaum. Psychiatrists apply the term "catatonia" in a rather vague manner to several discrete neurological phenomena bearing little or no relationship to each other. Thus "catatonia major" is applied to the spontaneous assumption of statuesque poses, whereas "catatonia minor" is used to include verbigeration, stereotypy and negativism. "Flexibilitas cerea" is a term frequently used for the clinical phenomenon in question. Amongst continental authors the word "Katalepsie" (or "catalepsie") is in favour, but its use in this country in a different sense and the possibility of confusion with cataplexy argue against its adoption. "Contraktionsnachdauer" and "Haltungsverrharen" are also at times used synonymously with Katalepsie.

In organic neurology catatonia is usually intimately associated with rigidity, the nature of which is pallidal rather than pyramidal.

The first question which arises in a discussion of the nature of catatonia concerns its relationship with rigidity. In cerebral arteriosclerosis, catatonia is essentially bound up with the phenomena of rigidity, and is not seen in patients with a normal muscle tonus. In various psychoses the association is less definite; in dementia præcox a rigidity may be demonstrable, but of an entirely different nature; psychical factors in all probability constitute the sole pathogenic agency and it is not necessary to postulate structural changes in the motor systems. Moreover, in the psychoses catatonia is quite often present in the absence of rigidity.

Demole claims to have produced catatonia in cats and rabbits experimentally by injecting solutions of sodium or potassium chloride which produced destructive lesions in the basal ganglia, and particularly in the thalamus.

Wilson [103], however, has produced evidence to show that catatonia may occur as a concomitant of a pyramidal type of spasticity. His patient was an elderly man who was admitted to hospital in a semi-conscious state twenty-four hours after a stroke. There was a right-sided hemiplegia with rigidity, and some degree of aphasia. The deep reflexes were increased on the right side; the plantars were both in reduced flexion, and a crossed plantar response was obtained from the right sole. When the patient was placed upon his left side, the right lower extremity was passively abducted at the hip and flexed to a right angle at the knee. This awkward position was maintained for three minutes. Two Jacksonian fits commencing in the right arm appeared on the following day. The diagnosis of cortical (submeningeal) hæmorrhage over the left ponto-parietal region was made and corroborated at autopsy.

There is but one neurological condition described, namely, cerebellar disease, where catatonia may occur in association with states of diminished muscle tonus. Although, contrary to general experience, Babinski [3] has emphasized a "catalepsie cérébelleuse" in the human subject, while Luciani, Thomas, Greggio, Borgherini and Gallerani have observed the same after experimental ablation of part or whole of the cerebellum in animals.

The ordinary cases of pallidal rigidity (exemplified by paralysis agitans, post-encephalitic Parkinsonism, progressive lenticular degeneration) show an increase in the degree of plastic (or postural) tonus. Many of them, as pointed out by Foerster, tend to fix the limb whatever muscle length is passively imposed (fixation-rigidity:

Adaptionsspannung). True catatonia, however, is not typically met with; as Wilson wrote [102], "catatonic phenomena have no place in the syndrome."

Catatonia, therefore, is a symptom which can appear in association with pyramidal or extrapyramidal types of rigidity, but which is independent thereof. It may occur as a psychotic manifestation unassociated with motor disability, although accompanied by a psychical type of rigidity. Lhermitte concludes that catatonia is the result as much of a suggestibility due to psychical disintegration as to a disorder of innervation resulting from pallidal destruction. Steck [91] regards catatonia as a link connecting organic with functional phenomena.

We may, therefore, speak of "motor" and "psychical" components of catatonia. Within the motor complex are included all the hypokinetic-hypertonic manifestations of pallidal disease together with a fixation-rigidity. Pallidal disease of itself is unassociated with catatonia, unless the psychical component is also present.

Marinesco [66] has suggested that the cerebellum might participate in the mechanism of catalepsy (catatonia) associated with Parkinsonism, and demonstrated lesions in the dentate and roof nuclei in fatal cases of acute epidemic encephalitis in which catalepsy had been a prominent symptom during life.

Defective mentation is an all-important agent in the production of catatonia, just as in arteriosclerotic rigidity. A disordered power of perception, lack of attention and retarded cerebration together contribute towards a definite ideational inertia. The patient is unable to grasp successive concepts if following too close on one another; if the suggestion takes the form of a command there will result a perseverated motor response. If, on the other hand, it takes the form of an attitude passively imposed upon a limb-segment, the posture tends to be maintained against gravity for an undue length of time. Either of two views may be hazarded to explain this: on the one hand, the patient may be unaware of the attitude of his limb in space, the proprioceptive impulses failing to reach consciousness on account of the dementia. In other words, the patient becomes for a while oblivious of the existence of his limb. Or, on the other hand, the patient's sensorium may be replete with the suggestion of the new attitude passively imposed, to the exclusion of fresh ideas. It is not until this initial suggestion wanes or becomes replaced by the painful impulses from the tiring muscles that the catatonic attitude is interrupted.

Chapter V.—Pathology.

Although the scope of this communication is essentially clinical, it is impossible to discuss arteriosclerotic Parkinsonism without reference to its pathology. Hence, the anatomical data available in the literature have been examined with a view to determining the extent to which a pure pathological picture is forthcoming. The subject will be discussed along general pathological lines, and then the correlation of structural with functional change will be examined.

General Pathological Considerations.

The nature of the pathological process underlying the arteriosclerotic types of Parkinsonism is by no means uniform. All manner of regressive changes may be encountered, primary as well as secondary. The pathological picture will vary, moreover, according to the degree of abruptness of the ischæmic process.

Detailed description of the pathology would be far beyond the scope of this paper. It will suffice to mention quite briefly the more important morbid processes which may be encountered. For the sake of convenience one may regard the cerebral changes under three heads: (1) gross vascular lesions; (2) minute vascular lesions; and (3) changes consequent upon old age. It is obvious that any combination of these may occur.

The gross vascular changes include macroscopic areas of hæmorrhage or softening, lacunes of cerebral disintegration, and the "état criblé." They also include alterations in the cerebral coverings: thus the dura may become thick and hardened, small areas of calcification are not uncommon, and actual ossification may be present. Changes in the leptomeninges include thickening and opacity of the pia-arachnoid; adhesions make it impossible to strip the meninges without damaging the cortex; in such cases a typical worm-eaten appearance results—the "état vermoulu" of Marie. Section through the cortex in such cases often reveals a peculiar "streaky" appearance, described by Neubürger [72]. This feature usually antedates the "état vermoulu," and is thought to be an earlier stage of the same process.

The weight of the brain is diminished, and in extreme cases it may weigh less than 1,000 grm. Very often there is a convolutional atrophy, which may be universal or localized. In contrast to Pick's disease, however, cortical atrophy never occurs as a solitary pathological manifestation. When the atrophy is more or less localized, the frontal lobe is most often affected, followed next in frequency by the temporal

lobe. Some degree of passive ventricular distension always accompanies atrophy of the parenchyma (hydrocephalus *ex vacuo*). Shrinkage of the basal ganglia may be obvious to the naked eye, and may prove histologically to be the result, not of mechanical pressure from the hydrocephalus, but of an actual diminution in the number of cells.

The minute vascular changes consist, firstly, in glial overgrowth, which may be diffuse or patchy. In the latter case the gliosis may be most obvious around the blood-vessels; at other times it appears tangentially in the white matter immediately underlying the cortex (= Binswanger's subcortical encephalitis). Globus [35], who studied the glial changes by the impregnation methods of the Spanish school, found a hyperplasia of the astrocytes. In the areas of softening, however, the astrocytes show every variety of regressive change up to total disintegration. During this process of atrophy their morphological characters may so alter as to resemble the amœboid cells of Alzheimer, or even "gitter" cells. Hortega cells are somewhat increased in number, and appear often in irregular aggregations (germinal centres). Alterations occur in their shape; some constitute the giant microglia cells of Cajal, others develop into true compound granular corpuscles. The oligodendroglia shows a slight generalized hyperplasia, except in the necrotic areas where these cells are few or absent.

Neuronal changes include disappearance of cells. The remaining cells may show shrinkage, nuclear eccentricity and defective absorption of stain. The maximum change is usually found in the third and fifth layers of the cortex. Pigmentary deposits of an argentophil nature are not uncommon. The neurofibrils may be irregularly or uniformly thickened and the individual processes become intermingled (Alzheimer's tangles). Around the blood-vessels there may be an infiltration of small round cells.

Weigert-Pal preparations usually show widespread, though not necessarily intense, alterations in the myelin sheaths. Thus the long fronto-pontine tracts are frequently abnormally pale. The lenticular nucleus is almost always affected, especially the pallidum and its connections, and there is a relative demyelinization in the subthalamic structures.

The changes consequent upon senility comprise some degree of neuronal disappearance, hyperplasia of the connective tissue and increase in the pigmentary elements. The cortical cells tend to disappear early, particularly in the deeper laminæ, and Purkinje cells may be absent from the cerebellar cortex (Bouman [7]). Lastly, the presence of senile

plaques in the cortical gray matter is characteristic. Despite the work of Bouman and Bok [8], who found plaques in the basal ganglia in a number of cases (nine out of ten), most writers have stated that the central gray matter is rarely the seat of such change.

There is nothing specific in the character or distribution of the vascular alterations in this particular variety of arteriosclerosis. In most instances the larger arteries of the base show the maximum change, but in a few cases (cf. Claude and Cuel) the capillaries may be affected to a greater degree.

In those cases in which muscle changes, of the type of retractile myosclerosis, are prominent, the pathology is characteristic. Atrophy, pigmentation and plasmodial regression of the muscle fibres are found, and some of the fibres are hypertrophied. The connective tissue lying between the bundles and also between the individual fibres shows an enormous proliferation; fibrous or fatty tissue may replace some of the muscle fibres. Accumulations of small round cells distend the lymphatic spaces.

A number of cases also present evidence of disease in the peripheral nerve-trunks, consisting in parenchymatous degeneration with interstitial overgrowth, due to changes in the small nutritive blood-vessels. The nerve fibres are diminished in number and those that remain show pronounced atrophy. There is an increase in the peri- and endo-neural connective tissue. Changes in the vasa nervorum consist in a thickening of all the coats, especially the intima, and in places the lumen may be entirely blocked.

The distribution of the cerebral lesions in cases of arteriosclerotic Parkinsonism is characterized by an extreme diffuseness. Certain locations, however, are especially liable to be affected. Thus, in every instance the corpus striatum is the seat of widespread morbid change. Each of the constituent nuclei may be diseased, but the frequency with which the globus pallidus and the large striatal cells are affected is striking. The subthalamic centres are rarely specifically mentioned, though they are sometimes stated to be affected to a lesser degree. Certain writers have called attention to the implication of certain parts of the basal ganglia in cases with particular added symptoms; thus, Kleist has drawn attention to lesions in the thalamus in cases in which counterpull was a prominent feature; in Merzbach's cases of arteriosclerotic Parkinsonism, in which various speech iterations were present, there were marked changes in the caudate. Freund and Rotter have emphasized in their cases the presence of lesions in the dentate nuclei.

Where pyramidal and pseudo-bulbar signs were present, additional lesions are demonstrable in the white matter of the hemispheres, the internal capsule and the pons. Lesions in the cerebellum, particularly in the dentate nuclei, have been demonstrated in the cases belonging to the fifth clinical group, and also in some cases (cf. Freund and Rotter) in which no cerebellar signs were demonstrated during life.

The Pathology of Senile "Vorsteifung."

The pathological status of this particular syndrome is not easy to determine. According to Jakob, senile changes are found in the cortex such as plaques and Alzheimer's fibrillary thickenings. There is marked degeneration of the third and fifth layers, especially in the frontal and temporal lobes. In the striatum and pallidum there is a severe diffuse parenchymatous degeneration with glial increase. As in the idiopathic paralysis agitans, the large striatal cells suffer most. Unlike the ordinary case of senile dementia, plaques may occur in the basal ganglia; Alzheimer's tangles are not seen here. The pallidal network is filled with calcareous-like deposits which stain blue-black with hæmatoxylin and do not give a fat reaction. Changes in the locus niger are less severe in degree, but shrinkage of the cells, demyelinization and poverty of melanin are evident. Jakob differentiates this pathological picture from that in Alzheimer's disease by the presence of more severe changes in the striatum and pallidum.

Pathological diagnosis.—From the standpoint of the pathologist, most difficulty lies in distinguishing the arteriosclerotic types of Parkinsonism from idiopathic paralysis agitans and from the syphilitic and post-encephalitic varieties. Although the pathology of the true Parkinson's disease is far from being established, nevertheless there are certain rules which guide in differentiating it from arteriosclerotic Parkinsonism; in general terms, the latter diagnosis is suggested in the presence of any of the following features:—

(1) Naked-eye change in the basal ganglia or midbrain (hæmorrhages, softening, lacunes, "état criblé").

(2) Definite structural change in the walls of the blood-vessels (other than calcification).

(3) A marked degree of glial increase.

(4) Perivascular hæmorrhages.

(5) Lesions of similar type demonstrable elsewhere in the central nervous system (cortex, pons, cerebellum).

Although Löwy, and C. and O. Vogt, were inclined to make the

pathological diagnosis of paralysis agitans in the presence of macroscopic foci of disintegration (an "état criblé" of the caudate and lenticular nuclei) this view is not accepted by most other neuropathologists. Changes in the blood-vessels are slight or absent in idiopathic paralysis agitans (Ramsay Hunt, Lhermitte, Foix); and any marked thickening of the vessel wall or proliferation of its cell elements must be regarded with suspicion. An exception must be made in the case of "calcification" in the media and adventitia of the most oral blood-vessels of the globus pallidus—a change which Weston Hurst [39] has shown to occur in 50 per cent. of all brains. Lastly, the presence of a diffuse or scattered pathological process, not confined to the lenticular nucleus or to the subthalamic region, suggests an arteriosclerotic basis.

The pathological differentiation of arteriosclerotic Parkinsonism from syphilitic vascular disease of the striatum hinges on the character of the changes in the vessels and peri-arterial tissue. Thus, the syphilitic cases will be characterized by vascular changes affecting especially the endothelium and by lymphocytic infiltration of the vessel walls with exudation of small round cells into the Virchow-Robin spaces. Moreover, plasma cells are here and there visible, in contrast with the arteriosclerotic cases. In most of the recorded instances other widespread syphilitic lesions have been discovered, particularly in the cortex and spinal cord. It need hardly be pointed out that positive serological evidence of syphilis in no way invalidates the diagnosis of a co-existent arteriosclerotic process, and the cerebro-vascular lesions of a given case may be purely degenerative and not syphilitic, despite a positive Wassermann reaction.

The pathological features of post-encephalitic Parkinsonism are distinct from those of the arteriosclerotic varieties. Absence of high-grade vascular disease (other than "calcification" of the middle coat), absence of naked-eye focal lesions, and the presence of perivascular "cuffing" favour the former diagnosis. Some authorities have stressed the fact that in the post-encephalitic varieties the locus niger tends to be affected to a greater degree and more constantly than the globus pallidus, whereas the converse is sometimes held to be true for the arteriosclerotic types. The point of differentiation is not to be relied upon implicitly, however, as there may be widespread disease of the locus niger in the arteriosclerotic cases.

Pathological discussion.—It becomes obvious when we examine the pathological changes in this syndrome that the subject is bristling with difficulties. Discrepancies become apparent as soon as we cease to focus

upon the pallidum and take a comprehensive and commonsense view of the facts.

The first difficulty is the frequent presence of pathological lesions where none were suspected by the clinician; a few examples will suffice. In Urechia and Mihalescu's case, in which a softening was found in the corpus striatum, no striatal symptoms were present during life. Vincent [98] reported foci of softening limited to the lenticular nucleus and to the head of the caudate in a case of an arteriopath who had shown no striatal symptoms. Frets found softening in the oral part of the caudate and putamen, in a patient who had clinically no symptoms referable to the basal ganglia. A case recorded by Freund and Rotter (Group 3, Case 2) was found at autopsy to have, besides the ordinary cortical changes of senile dementia, severe vascular lesions in the pallidum and in the dentate nuclei. Clinically this patient showed only a few symptoms referable to the strio-pallidum, a fact which the authors found difficult to explain. Lastly, one might quote those cases in which severe vascular lesions in the lenticular nuclei have been found after coal-gas poisoning without any corresponding symptoms, and the bilateral pallidal softenings in fatal cases of pneumonia (Hadfield [108]) in which striatal disease was never suspected.

It is arguable, of course, that in some of these instances the examination during life was incomplete and that minor strio-pallidal symptoms might have been overlooked. This is a possibility in some cases, particularly where a state of coma has rendered difficult a neurological examination. But not all the discrepancies can be explained away in this fashion; there still remain cases where full clinical investigations have failed to demonstrate unequivocal basal ganglion symptoms.

Again, in correlating the pathological and clinical data in cases of senility, one is in doubt as to what exactly is understood by the term "normal" old age. Oseki [76], for example, has reported definite pathological lesions (lacunes, gliosis, fatty degeneration of cells) in the corpus striatum of ten senile patients (aged 70-85). All of these were reported as showing no abnormal neurological signs during life, but we do not know whether any distinction was drawn between healthy senescence and pathological senility, and how much rigidity and asthenia, and what degree of akinesis, were regarded as normal.

It may be conceded, therefore, that pathological changes are sometimes present, of which we do not find adequate clinical expression. It is less easy to gauge the frequency of the opposite phenomenon, that

is, whether cases occur that clinically suggest striatal disease, which cannot be substantiated pathologically. There are but few cases on record of this anomaly. A similar difficulty is met with where clinical evidences of bilateral disturbances of striatal function have been present although the pathological condition has been that of strictly unilateral disease. Noethe's case is an excellent example: Meissner's case of a right-sided cerebral tumour involving the basal ganglia was associated clinically with a bilateral catatonic-akinetic syndrome.

Of particular interest are those rare instances where a single pathological lesion has given rise to bilateral clinical signs of a different order in the two halves of the body. Thus, a solitary focus in the corpus striatum may be characterized by a contralateral hemiplegia with homolateral catatonic phenomena. In Rieger's case, for instance, a softening in the right corpus striatum was followed by a left hemiplegia and right-sided catatonia, while a patient of Kraepelin's developed, from a single pathological lesion, a contralateral hemiplegia and a homolateral catatonia.

Again, in cases where clinical evidences of bilateral strio-pallidal disease are associated with bilateral striatal lesions, the clinical signs may have been unequal in degree on the two sides without any corresponding anatomical asymmetry. Jakob's first case (No. XI) illustrates this point; in this patient the right side of the body was weaker and more rigid, and the muscles of the right side were harder on palpation, but the intensity of the pathology was approximately equal in the two hemispheres.

It is necessary to recall, moreover, that the presence of anatomical lesions does not necessarily entail abolition of function. Certain pathological changes, such as demyelination, glial increase, or perivascular cell infiltration, are not incompatible with physiological activity, and it is not until the process becomes widespread or disseminated, or until there is actual damage to the neuron, that permanent loss of function results. An association with the pathophysiology of disseminated sclerosis is at once suggested. The degree of suddenness with which the pathological changes arise probably influences the resulting clinical picture; thus, abrupt lesions accompanied by œdema and other temporary disturbances in the local vascularity, are probably associated with severe clinical manifestations which are not of permanent character. On the other hand, a gradual and progressive ischæmic process will lead to a permanent and steadily increasing disability. Lastly, in states of partial or relative ischæmia

the efficiency of the cerebral circulation will depend on numerous other variants, such as the degree of splanchnic distension, posture, sleep and exercise.

The frequency with which unilateral lesions are seen compared with the rarity of clinical manifestations of arteriosclerotic Parkinsonism confined to one side suggests the question whether bilateral vascular lesions are required before amyostatic symptoms become manifest. It is, of course, well known that a hemiplegic distribution of symptoms is common in paralysis agitans proper, and this probably corresponds to a unilateral pathological change. The nature of the causative lesion, however, is very different in this case; an atrophy of large pallidal cells is essentially a selective or systemic process, and is, unlike the the cruder vascular lesions, superimposed upon a full complement of neurons.

In assessing the probable effect of particular morbid processes it is necessary to recall the patchy nature of certain types of cerebro-vascular disease. As Dunlap [22] has pointed out, in cerebral arteriopathy the striatum may be "peppered" with lesions, each one of which is sufficient to abolish the function of the particular cells affected. The intervening areas are, however, immune and their physiological activities are unimpaired. The "état criblé" and the lacunes of cerebral disintegration are the best illustrations of a dissemination of small lesions with integrity of the intervening structures.

We are dealing, therefore, with a pathological process which is diffuse and which may be present as scattered islets occurring haphazard throughout the nervous system. Each individual focus may or may not be sufficient in itself to cause an alteration in function. There results, therefore, a disability which is probably not equivalent to the algebraic sum of the component lesions. Years ago Hughlings Jackson pointed out that the so-called "double hemiplegia" is not the equal of two hemiplegias, but is that plus something more. The same phenomenon is seen in other types of cerebro-vascular disease. Cerebral arteriopathy may be also compared with disseminated sclerosis, in that both diseases are characterized by a multiplicity of diffuse but discrete lesions with a resulting clinical picture. It is questionable whether one is justified in correlating pathology with clinical findings along purely anatomical avenues; or whether the dissolution of function does not take place along phylogenetic lines, as suggested by Brouwer [11]. If so, one must not expect to correlate a given symptom with a particular lesion; Brouwer has suggested that when the central nervous

system is affected by a multiplicity of diffuse lesions the end-result will be in accordance with Jackson's views of evolution and dissolution. Functions which are old in the phylogenetic sense will be spared, whilst the youngest physiological processes will be the first to suffer. A developmental explanation rather than a strictly anatomical one may hold true, therefore, for some of the cases of diffuse cerebro-vascular disease.

An explanation is obviously desirable of those cases in which bilateral clinical signs (either similar or dissimilar) occur as the result of a solitary unilateral lesion. When examined more closely, however, the isolation of the focus is more apparent than real; in other words, there may exist other pathological changes, single or multiple, and probably of a microscopic character, which influence profoundly the effect of subsequent gross lesions. In Rieger's case there was, in addition to a softening in the right corpus striatum, the characteristic pathological evidences of general paralysis; Kraepelin's patient had, besides a single focus of disease, a large internal hydrocephalus affecting the lateral ventricles of both hemispheres. In such cases there are multiple diffuse lesions which, of themselves insufficient to cause physical signs, are immediately made manifest on the addition of a single large focus.

Kleist has put forward an explanation along anatomical lines: the pallidum (and striatum) send impulses to both sides of the body, but especially to the opposite side, and small unilateral lesions therefore produce no clinical symptoms. On the other hand, larger one-sided lesions produce motor manifestations of contralateral distribution. Bilateral lesions of a gross character produce bilateral signs. Slight lesions in both striata give rise to psychomotor hyperkinetic manifestations in both halves of the body. The combination of a gross lesion in one striatum with a small lesion in the other produces a hemiplegia on the side opposite the larger focus, with psychomotor hyperkinesis of homolateral distribution.

An analogy is found in those rare cases of a contralateral hemiplegia with homolateral grasping and groping, apparently resulting from a single pathological lesion (e.g., Schuster). In such cases there are either multiple minor foci scattered throughout both hemispheres, or (as in the case of tumour) the opposite half of the brain is distorted by hydrocephalus or by direct pressure.

The possibility of correlating with precision the anatomical and clinical data, in view of the many difficulties enumerated, arises at this point. Numerous attempts have been made to deal with the problem,

but many of the conclusions are probably too schematic and too plausible. The available facts may be very briefly marshalled.

When senile or arteriosclerotic processes are limited to the cortex we find clinically a state of dementia without physical manifestations of Parkinsonism. Hence it may be argued that the dementia is the expression of cortical change, whether of the nature of senile plaques, cell atrophy or capillary fibrosis. In general terms it may also be stated that the degree of intellectual loss is directly proportional to the severity of the cortical change.

Recently, Rhein, Winkelman and Patten [82] have attempted to correlate the mental conditions in the aged with the anatomical distribution of the changes in the cerebral blood-vessels. Thus they associate disease of the arteries of large calibre with the clinical picture of "arteriosclerotic deterioration." Sclerosis of the small vessels is coupled with a "progressive arteriosclerotic psychosis." Disease of both large and small arteries is associated with "arteriosclerotic dementia." In a fourth group they place those cases in which the arterial changes are fibrotic rather than sclerotic in type; this pathological group comprises individuals whose mental faculties were preserved and the cases fell into the cadre of "senility." Unfortunately, the authors do not deal with the neurological aspect of their subject.

Some of the positive or active manifestations of dementia such as hyperkineses of a complicated or "psychomotor" type, the negativistic manifestations of "counterpull," and diverse movements of clutching, grasping and groping, require explanation. There is but little unanimity here. Earlier workers associated many of these phenomena with disease of the basal ganglia, without specifying any particular localization. Adie and Critchley have, however, referred the grasping movements to disease of the frontal lobe. Schuster, who formerly regarded striatal disorder as their cause, modified his earlier opinion and suggested a combined frontal and striatal dysfunction, the major importance being attached to the frontal lesions. Kleist stated that psychomotor disorders, although frequently associated with changes in the frontal lobes, do not result therefrom, but rather from a disordered balance of function between the individual ganglia of the corpus striatum. Forced grasping and allied phenomena are, in his opinion, part of the wider process of counterpull, which he associates with disease of the thalamus, releasing a lower affective centre in the caudal oblongata.

Further difficulty is encountered in correlating the hypokinetic-hypertonic syndromes with an anatomical basis. Whether it is justifi-

able to regard akinesis and rigidity as necessarily associated one with the other is doubtful. The whole trend of modern opinion is to the contrary. Foerster says quite definitely: "to identify the hypokinetic (or akinetic) syndrome with rigidity or 'Fixationsspannung' is to ignore the complexity of the problem." It is well known that the two symptoms are not necessarily co-existent, for while akinesis usually accompanies rigidity, it is often demonstrable in cases in which there is no increased tonus, and conversely, a state of pathological restlessness (or akathisia) can accompany a Parkinsonian syndrome. One must, therefore, dissociate these two symptoms for the purpose of discussion. Although it is not correct to associate rigidity entirely with poverty of movement, one is probably justified in regarding hypokinesis as part of the bradykinetic syndrome of Cruchet.

Most continental writers (Lotmar [63], C. and O. Vogt [99], Kleist) have tended to associate the Parkinsonian akinesis with a disappearance of the large cells of the striatum, or of the locus niger, or both. Thus, Kleist correlates poverty of associated and single movements, particularly those occurring in the periphery of the limbs and in the face, with disease of the locus niger, and especially the zona reticularis. On the other hand, disease of the caudate and external pallidum produces a diminution or absence of the higher expressive and symbolic automatisms. Jakob associates akinesis with disease of the small ganglion cells of the striatum. Lewy has departed somewhat from the traditional views in suggesting that part at least of the hypokinesia in Parkinsonism results from disease of the frontal lobes.

It is obvious, moreover, that akinesis is a manifestation of many types of nervous and even extraneural disease. A striking paucity of movement (thought not paralysis) can occur in cerebellar disease, in lesions of the sensory cortex, in stuporose states, as well as in painful and other affections of the peripheral nerves, muscles and joints. Kinnier Wilson is emphatic on this point: . . . . "akinesis, or poverty of movement," he states, "obviously may arise at one or more of the lower, middle or highest physiological neural levels (in Hughlings Jackson's sense), a possibility which renders invalid its ascription to the corpus striatum alone."

The question of rigidity in arteriosclerotic Parkinsonism has already been discussed, and it has been emphasized that besides the pallidal component (resulting from the loss of the large striatal cells) other important factors contribute to the increased tonus. One recalls, too, that Stief quotes Jakob and the Vogts in suspecting cortical changes of

contributing to the rigidity in cases of Parkinsonism. There is abundant pathological evidence linking disease of the palæostriatum with the appearance of a distinctive type of rigidity. One interesting point for discussion hinges, however, on the relative importance of pallidal as opposed to nigral changes. Whereas the former are the more obvious in idiopathic Parkinsonism, the latter are all-important in the post-encephalitic varieties.

In the arteriosclerotic types co-existent changes in both pallidum and locus niger are often described. But in certain instances it is clear that pallidal lesions may exist without any corresponding disease of the locus niger. There is only one record of the opposite condition, namely, morbid processes in the locus niger with a healthy pallidum, in a case of arteriosclerotic Parkinsonism (cf. Case 5, Freund and Rotter). The close anatomo-physiological and developmental association between these two structures renders controversy as to their relative importance of theoretical rather than of practical value.

Some authorities have considered the hypertonic-akinetic syndrome as a whole and have carried the process of correlation still further. Kleist, for example, considers striatal function as follows: (1) gross automatisms (i.e. mass movements of the whole body) are regulated by the subthalamic structures and the internal pallidum; (2) finer automatisms belong to the putamen and locus niger; and (3) finest automatisms (expressive and symbolic movements) are subserved by the caudate and external pallidum. Symptoms due to lesions of groups (1) and (2) cause "myostatic disorders," whereas affections of (3) produce "psychomotor" disturbances.

Kleist goes further, and supports Jakob and C. & O. Vogt in ascribing to the basal ganglia a somatotopy, or anatomical representation of body segments. Thus the head, face and the organs of speech are said to lie farthest forward in the most cephalad segments of the pallidum, putamen and caudate, followed next by arm and trunk, the leg centres being the most caudal.

Other views have been held with regard to the pathogenesis of the arteriosclerotic rigidity-syndrome, besides involvement of the striatum. It will be recalled that Foerster originally suggested disease of the cerebellum and its connections. In his later communications Foerster refers to his earlier belief and points out the many clinical resemblances between the arteriosclerotic rigidity and syndromes of fronto-ponto-cerebellar origin (hypokinesis, rigidity, flexor attitudes, bradykinesis, catatonia).

An interesting point has been raised by Freund and Rotter. They believe the pathological process in some of their cases to represent a hitherto undescribed combined system-disease of the strio-pallidal-dentate-rubral-peduncular pathways. In this way the red nucleus is cut off from strio-pallidal as well as from cerebellar influences. The authors speculate as to the possible clinical significance of a physiological isolation of the red nucleus (cf. Munk's "Isolierungsprinzeps.")

Certain interesting problems arise regarding the origin of the early and severe joint and periarticular changes in cerebral arteriosclerosis. We have already hinted at an association between chronic arthritis deformans and a state of pseudo-Parkinsonism, a connection which, since the writings of Charcot, has received no little attention in France. A detailed study of "le syndrome pallidal du rheumatisme chronique déformant," as it is called, would be beyond the scope of this paper, except in its relationship with the arteriopathic types. Contractures and joint changes appear early and may become severe in cases of arteriosclerotic Parkinsonism, and the possibility arises as to whether these complicating features are determined solely by decubitus, faulty nursing and other similar factors. It is conceivable that the presence of cerebral disease has a more direct and causal relationship. Foerster, in describing the anomalies of attitude and the deformities of the hands and extremities in this syndrome, believes they exist independently of contractures, and are due to an independent, specific, flexing factor. Freund and Rotter[30] affirm quite definitely that in extrapyramidal manifestations of advanced age joint deformities of cerebral origin occur, which in outward form simulate those of chronic progressive polyarthritis.

It is obvious from a consideration of the foregoing attempts at associating anatomical and clinical data that no satisfactory conclusion is possible. Indeed it is fair to say that the study of arteriosclerotic Parkinsonism has so far thrown little light upon the problem of striatal physiology, and in view of the difficulties peculiar to cerebral arteriosclerosis in correlating structural with functional change, it is doubtful whether any great help is to be expected in this direction.

Such information as has been available tends to argue against a conception of the corpus striatum as the sole, or even the most important, site of disease in arteriosclerotic rigidity-syndromes. This view confirms Kinnier Wilson's views expressed as follows: . . . "my clinical studies have impressed me with the belief . . . that striatal symptomatology and function must be comparatively simple; and they

have forced me to the conclusion that the unwieldy and top-heavy symptom-complex which has gradually come to be erected on the ganglia must be vigorously stripped of non-essentials."

Senile Rigidity; Inter-relationship with Senility, Dementia, Arteriosclerotic Rigidity and Parkinson's Disease.

Other problems present themselves for discussion at this stage, and the claims of Jakob's senile rigidity as a clinical entity will require consideration. Secondly, the relationship of this syndrome to other varieties of Parkinsonism (both idiopathic and arteriosclerotic) and the association of these diseases with senility and senile dementia afford interesting speculation. Some have actually assumed a unitary conception for these morbid states, associating them with an identical pathogenic basis, namely, an involutional process differing only in its anatomical location.

The question of the status of Jakob's disease may be considered first. Jakob isolated certain types of senile dementia, closely allied to Alzheimer's disease, in which rigidity is a prominent manifestation. In such cases the pathological changes are dominant in the striatal parenchyma; cortical processes of simple senile dementia are also demonstrable but in lesser degree. Lhermitte, however, is opposed to the isolation of a senile variety of rigidity from the arteriosclerotic types; mental enfeeblement, he points out, may be equally conspicuous in the arteriopathic type of pallidal rigidity. But Lhermitte does not discuss the propriety of considering under the title of senile muscular rigidity those cases in which no clinical or pathological evidence of arteriosclerosis is forthcoming. Such cases cannot be classed as arteriosclerotic Parkinsonism. They differ too from idiopathic paralysis agitans in their later onset, the absence of tremor, and the outstanding dementia which often antedates the pallidal signs. The pathological differences centre in the relative severity of cortical changes.

The akinetic-hypertonic senility-syndromes may be regarded as exaggerations of the physiological movement disorders of old age. As Stief points out, the frontiers between physiological and pathological activities (the "physioklise" and "pathoklise" of the Vogts) are here particularly intangible.

We may now pass to the relationship between senile processes and the occurrence of dementia, arteriosclerotic Parkinsonism and paralysis agitans. An all-important problem naturally arises as to the relationship between senile and arteriosclerotic processes in general: whether

the cerebrum is actually as old as its blood-vessels; or whether the pathological changes of the senium are distinct from those of the cerebrovascular system. All the evidence goes to suggest that the structural changes of old age are independent of arterial degeneration. Although frequently associated, the senile brain and the arteriopathic brain are independent entities. As Stief remarks, the ageing of the central nervous system is a process *sui generis* associated with, but not dependent upon, the old age changes in the vascular system.

It is clear, therefore, that there must be distinctions between senile and arteriosclerotic dementia, and between senile and arteriosclerotic Parkinsonism. The frontiers are ill-defined, however, and the two processes are so often combined that it obviously becomes difficult at times to relegate a particular case to its proper category. All who have studied the subject, whether along clinical or pathological lines, insist that there are transition forms between the various involutional disorders of the strio-pallidum and cortex. Jakob speaks of intermediate clinical and histological types which link up paralysis agitans, via Alzheimer's disease, with senile rigidity plus dementia on the one hand, and on the other with arteriosclerotic rigidity. Stief is inclined to place paralysis agitans among the neurological manifestations of senility. In this way he associates himself with the conception of Jelgersma and Lewy in regarding Parkinson's disease as the result of senile disintegration with fortuitous incidence upon the basal ganglia. The involutional disorders of the cerebrum may, therefore, be grouped according to their location into the following schema of Stief's:—

(*a*) Predominating in cortex	.. =	*Senile dementia.*
(*b*) Predominating in basal ganglia	=	*Paralysis agitans (without psychosis).*
(*c*) Affecting cortex and basal ganglia	=	*Senile chorea. Paralysis agitans with mental change. Senile rigidity. Alzheimer's disease.*

In the latest exposition of the pathology and genesis of Parkinson's disease, Foix and Nicolesco [27] take up an open attitude with regard to the association with old age. They make the statement, however, that paralysis agitans appears at times as the result of an abnormal localization of the processes of senility.

Conclusions.

The object of this communication is to draw attention to a variety of Parkinsonism due to cerebral arteriosclerosis.

Although cerebro-vascular disease may give rise to the complete picture of Parkinson's disease, incomplete forms are commoner. All gradations occur, from the mildest degree of hypokinesis and

hypertonus (= arteriosclerotic rigidity) up to forms which are barely distinguishable from classical paralysis agitans.

For convenience of description one may subdivide the cases of arteriosclerotic Parkinsonism into five clinical types: (1) early cases characterized by some immobility of expression and short-stepping gait; (2) cases forming part of the pseudo-bulbar syndrome; (3) cases associated with marked intellectual defect; (4) pyramido-pallidal syndromes; and (5) cerebello-pallidal syndromes.

There are several clinical points of distinction between the arteriosclerotic varieties of Parkinsonism and cases of idiopathic paralysis agitans:—

Symptoms may commence suddenly in the arteriosclerotic cases, although an insidious onset is more usual. The progression is more rapid and may proceed by a series of abrupt exacerbations.

The age of onset is approximately the same in the two conditions, but an unusually early or a very late age for commencement of symptoms suggests a vascular basis.

In the arteriopathic cases tremor is usually absent; the muscles feel firmer to the touch; and the rigidity is often characterized by a superadded tendency towards catatonia.

Many of the arteriosclerotic cases (e.g., those in Group 2) have "bulbar" signs and emotional incontinence. A large number, too, show a more or less profound dementia.

The presence of other focal cerebral symptoms (of aphasic, apraxic, cerebellar or pyramidal nature) argues in favour of an arteriosclerotic basis.

Evidence of disease in the cerebral or peripheral blood-vessels is present in the arteriosclerotic varieties; the blood-pressure is often high, but in the senile or decrescent types of arterial degeneration the tension may be low.

The pathological appearances vary greatly in character and diffuseness; the essential features comprise lesions in the globus pallidus, and, to a lesser extent, in the substantia nigra, directly consequent upon vascular disease.

Pallidal lesions must not be regarded as the sole responsible agents in the clinical appearances, for changes at other levels can be demonstrated as contributing towards the rigidity. Thus, mental impairment, pyramidal disease, changes in the peripheral nerves, and in the muscles, tendons, joints, and blood-vessels of the extremities, all play a part in producing a hypertonic-hypokinetic syndrome.

By isolating an arteriosclerotic variety, support is given to the conception of Parkinsonism as a syndrome which may occur under numerous pathological circumstances. It is the site, rather than the nature of the disease, which produces the characteristic clinical picture.

In conclusion, it is a pleasure to express my indebtedness to Dr. S. A. Kinnier Wilson for his kind and valuable criticisms. My thanks are also due to Drs. Collier, Holmes, Walshe and Feldman for permitting me to quote cases under their care.

REFERENCES.

[1] Adie, W. J., and Critchley, M. "Forced Grasping and Groping," *Brain*, 1927, **50**, 142.

[2] Alzheimer. "Die Seelenstörungen auf arteriosklerotischen Grundlage," *Allg. Zeitschr. f. Psychiatr.*, 1902, **59**, 695.

[3] Babinski, J. "Quelques documents relatifs à l'histoire des fonctions de l'appareil cérébelleux et de leurs perturbations," *Rev. Mens. de Méd. Int. et de Thérap.*, 1909 (May), p. 6.

[4] Bard, L. "Des contractures post-hémiplégiques pseudoprécoces," *Sem. Méd.*, 1907, **27**, 61.

[5] v. Bechterew. "Hemitonia post-apoplectica," *Deutsch. Zeitschr. f. Nervenheilk.*, 1899, **15**, 437.

[6] Boettiger. "Ueber extracapsuläre Hemiplegien inbesondere über 'Hemihypertonia apoplectica,'" *ibid.*, 1921, **68-69**, 165.

[7] Bouman, L. "Die Axonschwellungen der Purkinjeschen Zellen, inbesondere bei Dementia Senilis," *Zeitschr. f. d. ges. Neurol. u. Psychiatr.*, 1928, **113**, 379.

[8] Bouman, L., and Bok, S. T. "Senile Plaques im Corpus Striatum," *ibid.*, 1923, **85**, 164.

[9] Brissaud, E. "Leçons sur les maladies nerveuses," Paris: Masson, 1895, p. 486.

[10] *Idem.* "Leçons," 2me série, Paris: Masson, 1899, p. 305.

[11] Brouwer, B. "Anatomical, Phylogenetical and Clinical Studies on the Central Nervous System," Baltimore, 1927.

[12] Buzzard, E. F., and Barnes, S. "A Case of Chronic Progressive Double Hemiplegia," *Rev. Neurol. and Psychiatr.*, 1906, **4**, 192.

[13] Catola. "Étude clinique et anatomo-pathologique sur les lacunes de désintégration cérébrale," *Rev. de Méd.*, 1904, **24**, 778.

[14] Claude, H., and Alajouanine, Th. "Hypertonie généralisée avec troubles d'aspect pseudobulbaire, rire et pleurer spasmodique chez un adulte. Localisation pallidale probable," *Rev. Neur.*, 1922, **29**, 567.

[15] Claude, H., and Cuel, J. "La meiopragie cérébrale par angiosclérose précoce sans ischæmie en foyer (forme de démence présenile artério-scléreuse), *L'Encéphale*, 1927, **22**, 161.

[16] Collins, J. "A Case of Cortical Cerebral Arterio-sclerosis with Distinct Focal Symptoms," *The Post-Graduate*, 1905, **20**, 465.

[17] *Idem.* "A Definite Clinical Variety of Cerebral Arteriosclerosis," *Journ. Nerv. and Ment. Dis.*, 1906, **33**, 750.

[18] Cones, W. Pearce. "Note on a Case of Paralysis Agitans and Cerebral Arterio-sclerosis," *Bost. Med. and Surg. Journ.*, 1911, **164**, 755.

[19] Critchley, M. "On Palilalia," *Journ. Nerv. and Psychopath.*, 1927, **8**, 23.

[20] Crouzon, Dereux and Kenziger. "Paralysie pseudobulbaire d'origine protuberantielle (association d'un syndrome pseudobulbaire et d'un syndrome cérébelleux)," *Rev. Neur.*, 1925, **32(2)**, 747.

[21] Demole, V. "Catatonie expérimentale," *ibid.*, 1927, **34**(1), 861.
[22] Dunlap, C. B. "Structural Changes in Huntington's Chorea," *Brain*, 1927, **50**, 631.
[23] Farran-Ridge, C. "Some Symptoms referable to the Basal Ganglia occurring in Dementia Præcox and Epidemic Encephalitis," *Journ. Ment. Sci.*, 1926, **72**, 513.
[24] Ferrand, J. "Essai sur l'hémiplégie des vieillards," *Thèse de Paris*, 1902.
[25] Foerster, O. "Die arteriosklerotische Muskelstarre," *Allg. Zeitschr. f. Psychiatr.*, 1909, **66**, 902.
[26] *Idem.* "Zur Analyse u. Pathophysiologie der striaren Bewegungsstörungen," *Zeitschr. f. d. ges. Neur. u. Psychiatr.*, 1921, **73**, i.
[27] Foix, Ch., and Nicolesco, J. "Les noyaux gris centraux et la région mésencéphalo-sous optique." Paris: Masson, 1925.
[28] Franceschi, F. "Polineurite et arterio-sclerosi del sistema nervoso centrale e periferico," *Riv. di Pat. nerv. e ment.*, 1903, **8**, 193.
[29] Freund, C. S., and Roiter, R. "Extrapyramidale Bewegungsstörungen im höheren Alter," *Arch. f. Psych.*, 1927, **81**, 5.
[30] *Idem.* "Ueber extrapyramidale Erkrankungen des höheren Alters mit einem Beitrag zur Pathogenese seniler Parenchymveränderungen," *Zeitschr. f. d. ges. Neur. u. Psychiatr.*, 1928, **115**, 198.
[31] Fumet, P. "Contribution à l'étude des myopathies séniles primitives," *Thèse de Paris*, 1922.
[32] Garbini, G., and Rossi, U. *Annali di Manicomio provinciale di Perugia*, 1909, **3**, 140.
[33] Gaussel, A. "Contractures précoces et permanentes dans un cas d'hémiplégie de l'adulte," *Nouv. Icon. de la Salpêtr.*, 1905, **18**, 241.
[34] van Gehuchten, P. "Hémiplégie avec aspect figé de la face," *Rev. Neur.*, 1925, **32**(**2**), 794.
[35] Globus, J. H. "Glia Response in Chronic Vascular Disease of the Brain," *Arch. Neur. and Psych.*, 1928, **20**, 14.
[36] Golla, L. "The Objective Study of Neurosis" (Croonian Lecture), *Lancet*, 1921, **2**, 115, 215, 265, 373.
[37] Hall, A. J. "Rate of Movement in Post-encephalitic Parkinsonism," *ibid.*, 1927, **2**, 1009.
[38] Holmes, G. "On Certain Tremors in Organic Cerebral Lesions," *Brain*, 1904, **27**, 327.
[39] Hurst, E. Weston. "On the So-called Calcification in the Basal Ganglia of the Brain," *Journ. Path. and Bact.*, 1926, **29**, 65.
[40] Jackson, J. Hughlings. "Softening of the Brain," *Lancet*, 1875, **2**, 335.
[41] *Idem.* "On Cerebral Paresis or Paralysis with Cerebellar Tremor or Rigidity," *Med. Examiner*, 1878, **3**, 266.
[42] Jakob, A. "Die extrapyramidale Erkrankungen," Berlin: Julius Springer, 1923, p. 126.
[43] James, G. W. B. "Cerebral Arteriosclerosis," *Proc. Roy. Soc. Med.* (Sect. Psych.), 1926, **19**, 30.
[44] Janischewsky, A. "Un cas de maladie de Parkinson avec syndrome pseudo-bulbaire et pseudo-ophthalmoplégique. Quelques considérations sur la pathogène de cette maladie," *Rev. Neur.*, 1909, **17**, 823.
[45] Jarkowski, J. "Kinésie paradoxicale des Parkinsoniens," Paris: Masson, 1925.
[46] Kashida. "Ueber Gehirnarteriosklerose des früher Alters, und ueber die Kombination von corticalen, pyramidalen u. extrapyramidalen Symptomen bei der Gehirnarteriosklerose," *Zeitschr. f. d. ges. Neurol. u. Psychiatr.*, 1924, **94**, 659.
[47] Kleist, K. "Die psychomotorischen Störungen u. ihr Verhältniss zu den Motiliätsstörungen bei Erkrankungen der Stammganglien," *Monatsschr. f. Psychiatr. u. Neurol.*, 1922, **52**, 253.
[48] *Idem.* "Bewegungsstörungen u. Bewegungsleistungen der Stammganglien des Gehirns," *Die Naturwissenschaften*, 1927, **15**, 973.
[49] *Idem.* "Gegenhalten (motorischen Negativismus) Zwangsgreifen u. Thalamus Opticus," *Monatsschr. f. Psychiatr. u. Neurol.*, 1927, **65**, 317.
[50] Lejonne, P., and Lhermitte, J. "Étude sur les paraplégies par rétraction chez les vieillards," *Nouv. Icon. de la Salpêt.*, 1906, **19**, 255.

[51] Ley, R. A. "Forme atypique d'atrophie cérébelleuse ayant évolué en syndrome rigide," *Journ. de Neur. et de Psych.*, 1925, **25**, 92.
[52] Lhermitte, J. "Sur une forme spéciale de myopathie sénile," *Trib. méd.*, 1906.
[53] *Idem.* "Etude sur les paraplégies des vieillards," *Thèse de Paris*, 1907.
[54] *Idem.* "Les syndromes striées du vieillard," *Rev. Neur.*, 1922, **29**, 406.
[55] *Idem.* "La myosclérose retractile des vieillards et ses rapports avec le syndrome acinéto-hypertonique," *L'Encéphale*, 1928, **23**, 89.
[56] *Idem.* "La striatite syphilitique primitive," *La Médecine*, 1928, **9**, 349.
[57] Lhermitte, J., and Cornil, L. "Syndrome strié à double expression symptomatique; pseudobulbaire et parkinsonienne," *Rev. Neur.*, 1921, **28**, 299.
[58] *Idem.* "Recherches anatomiques sur la maladie de Parkinson," *ibid.*, 1921, **28**, 587.
[59] Lhermitte, J., and Cuel, L. "Forme ponto-cérébelleuse de la paralysie pseudobulbaire," *ibid.*, 1921, **28**, 364.
[60] Lhermitte, J., and Kyriaco, N. "La forme ponto-cérébelleuse de la paralysie pseudobulbaire," *Gaz. des Hôp.*, 1927 (vol. centennaire), 69.
[61] Lhermitte, J., and McAlpine, D. "A Clinical and Pathological Résumé of Combined Disease of the Pyramidal and Extra-pyramidal Systems, with Special Reference to a New Syndrome," *Brain*, 1926, **49**, 157.
[62] Liljestrand, G., and Magnus, R. "Ueber die Wirkung des Novokains auf den normalen u. den tetanusstarren Skelettmuskel u. über die Entstehung der lokalen Muskelstarre beim Wundstarrkrampf," *Arch. f. d. ges. Physiol.*, 1919, **176**, 168.
[63] Lotmar, F. "Die Stammganglien u. die extrapyramidalemotorischen Syndrome," Berlin: Springer, 1926.
[64] Mackintosh, Ashley. "Bulbar Symptoms in Paralysis Agitans," *Scott. Med. and Surg. Journ.*, 1903, **13**, 325.
[65] Marie, P., and Foix, Ch. "Les syncinésies des hémiplégiques," *Rev. Neur.*, 1916, **23**(**1**), 3, and **23**(**2**), 145.
[66] Marinesco, G. "Contributions à l'étude de l'encéphalite épidémique," *ibid.*, 1921, **28**, 11.
[67] Marinesco, G., and Nicolesco, M. "A propos des modifications du tonus postural et de l'apparition du signe de Babinski consécutive aux injections de scopolamine dans les hypertonies extrapyramidales," *ibid.*, 1927, **34**(**1**), 246.
[68] Martini, P., and Isserlin, A. "Paralysis Agitans, Tetanie und Arteriosklerose," *Klin. Wochenschr.*, 1922, **1**, 510.
[69] Mella, H., and Katz, S. E. "Neurosyphilis as an Etiological Factor in the Parkinsonian Syndrome," *Journ. Nerv. and Ment. Dis.*, 1924, **59**, 225.
[70] Merzbach, A. "Die Sprachiteration u. ihre Lokalisation bei Herderkrankungen des Gehirns," *Journ. f. Psychiatr. u. Neurol.*, 1928, **36**, 210.
[71] Monier-Vinard and Dalsace. "Syndrome pallidal," *Rev. Neur.*, 1921, **28**, 371.
[72] Neubürger, K. "Ueber streifenförmige Erkrankungen der Grosshirnrinde bei Arteriosklerose," *Zeitschr. f. d. ges. Neurol. u. Psychiatr.*, 1926, **101**, 452.
[73] Newmark, L. "A Lesion in the Putamen," *Journ. Nerv. and Ment. Dis.*, 1919, **49**, 97.
[74] Noethe. "Ueber einen Fall von motorischen Apraxie," *Arch. f. Psychiatr.*, 1913, **52**, 1043.
[75] Orzechowski. "De l'ataxie dysmétrique des yeux," *Journ. f. Psychiatr. u. Neurol.*, 1927, **35**, 1.
[76] Oseki. "Ueber die Veranderungen des Striatums in normalen Senium," *Arbeit. neurol Institt. Wiener Univ.*, 1924, **26**, 339.
[77] Pfeiffer, R. "Ein klinischer Beiträg zur Lehre von der Hemitonia Apoplectica (Bechterew)," *Neurol. Centralbl.*, 1901, **30**, 386.
[78] Pickett, W. C. "A Case of Arteriosclerosis of the Nervous System," *Journ. Nerv. and Ment. Dis.*, 1905, **32**, 182.
[79] Pinéas, H. "Klinischer u. anatomischer Befund eines Falles von Kohlenoxydvergiftung," *Zeitschr. f. d. ges. Neurol. u. Psychiatr.*, 1924, **93**, 47.
[80] Raymond, F., and Alquier, L. "Sur un cas de paralysie pseudobulbaire," *Nouv. Icon. de la Salpêt.*, 1907, **20**, 371.

[81] Reiter, P. J. "Extrapyramidal Motor Disturbance in Dementia Præcox." *Acta Neuro-Psych.*, 1926, **1**, 287.
[82] Rhein, J. H. W., Winkelmann, W., and Patten, C. A. "Mental Conditions in the Aged," *Arch. Neurol. and Psychiat.*, 1928, **20**, 329.
[83] Rosenfeld. "Ueber Skopolaminwirkungen am Nerven-system," *Munch. med. Wochenschr.*, 1921, **31**, 971.
[84] Rowland, R. "On the Nature and Treatment of Softening of the Brain," London, 1851.
[85] Schlesinger, H. "Ueber eine durch Gefässerkrankungen bedingte Form der Neuritis," *Neurol. Centralbl.*, 1895, **14**, 578 and 634.
[86] Schuster, P., and Pineas, H. "Weitere Beobachtungen über Zwangsgreifen u. Nachgreifen und deren Beziehungen zu ähnlichen Bewegungsstörungen," *Deutsch. Zeitschr. f. Nervenheilk.*, 1926, **91**, 16.
[87] Sicard, J. A. "Parkinsonisme et rheumatisme chronique," *Rev. Neur.*, 1921, **28**, 682.
[88] Sicard, J. A., and Paraf. "Syndrome strio-pyramidal," *ibid.*, 1921, **28**, 295.
[89] Signorelli, E. "Patogenesi del nistagmo palato-faringo-laringeo. Contributo-anatomo-clinico," *Riv. di Patol. nerv. e ment.*, 1927, **32**, 441.
[90] Souques, M. A. "Formes cliniques des syndromes parkinsoniens," *Rev. Neur.*, 1921, **28**, 562.
[91] Steck, H. "Les syndromes extrapyramidaux dans les maladies mentales," *Arch. suisses de Neur. et de Psych.*, 1926, **19**, 195; *ibid.*, 1927, **20**, 92.
[92] Stief, A. "Beiträge zur Histopathologie der senilen Demenz, mit besonderer Berücksichtigung der extrapyramidalen Bewegungstörungen," *Zeitschr. f. d. ges. Neur. u. Psychiatr.*, 1924, **91**, 879.
[93] Stoddart, W. H. B. "Motor Symptoms of Mania and Melancholia," *Lancet*, 1904, **1**, 639.
[94] Urechia, C. I. "La Syphilis peut-elle reproduire le Syndrome de Parkinson?" *Rev. Neur.* 1921, **28**, 581.
[95] Urechia, C. I., Mihalescu, S., and Elekes, N. "La rigidité artério-scléreuse et le syndrome pyramido-pallidal," *Arch. Internat. de Neurol.*, **42**, 161,
[96] Urstein. [Quoted by P. J. Reiter. "Nogle Undersøgelser over Sukkerstofskiftet ved Psychoser," København: Levin and Munksgaard. 1925.]
[97] Verger, H., and Cruchet, R. "Les états parkinsoniens et le syndrome bradykinétique." Paris: Baillière et Fils, 1925.
[98] Vincent, Cl. "Foyers de ramollissement limités au noyau lenticulaire et à la tête du noyau caudé—Aucun symptome strié," *Rev. Neur.*, 1925, **32**, 194.
[99] Vogt, C. and O. "Zur Lehre der Erkrankungen des striären Systems," *Journ. f. Psychiatr. u. Neur.*, 1920, **25**, 631.
[100] Walshe, F. M. R. "Observations on the Nature of the Muscular Rigidity of Paralysis Agitans and on its Relationship to Tremor," *Brain*, 1924, **47**, 159.
[101] *Idem.* "On Variation in the Form of Reflex Movements, notably the Babinski Plantar Response, under Different Degrees of Spasticity and under the Influence of Magnus and de Kleijn's Tonic Neck Reflex," *Brain*, 1923, **46**, 281,
[102] Wilson, S. A. Kinnier. "Disorders of Motility and Muscle Tone" (Croonian Lectures), *Lancet*, 1925, **2**, 1, 53, 169, 215, 268.
[103] *Idem.* "Modern Problems in Neurology." London: Arnold, 1928, p. 200.
[104] Wilson, S. A. Kinnier, and Cobb, S. "Mesencephalitis syphilitica," *Journ. Neur. and Psychopath.*, 1924, **5**, 44.
[105] Wladyezko, S. "Catatonie comme conséquence des troubles organiques des noyaux gris centraux," *Folia Neuropath.*, Estonia, 1925, **3**, 1,
[106] Wohlfahrt, S. S. "Pallido-striäre Symptome bei Lues in den basalen Ganglien des Gehirns," *Zeitschr. f. d. ges. Neur. u. Psychiatr.*, 1927, **108**, 115
[107] Young, A. W. "A Clinical Analysis of an Extra-pyramidal Syndrome: Paralysis Agitans plus Post-encephalitic Parkinsonism," *Journ. Neur. and Psychopath.*, 1927, **8**, 9.
[108] Hadfield. "Siderosis of the Globus Pallidus; its Relation to Bilateral Necrosis," *Journ. Pathol. and Bacteriol.*, 1929, **32**, 135.

A CASE OF THE PROGRESSIVE HYPERTROPHIC POLYNEURITIS OF DEJERINE AND SOTTAS, WITH PATHOLOGICAL EXAMINATION.

BY R. S. DE BRUYN

AND

RUBY O. STERN.

(From the Wards of Guy's Hospital and the Pathological Laboratory of the National Hospital, Queen Square.)

Introduction.

This disease, of which we have a new example to describe, is undoubtedly a rare one. We have been able to find in the literature only twelve cases with histological verification, and besides these fourteen clinical records. Of these latter, six, as we shall point out later, are of doubtful value.

The history of the disease begins with a paper by Dejerine and Sottas [3] in 1893, whose heading we quote in full so that we may explain our own choice of title. Their title reads "Sur la névrite interstitielle, hypertrophique et progressive de l'enfance, affection souvent familiale et à début infantile, caracterisée par une atrophie musculaire des extrémités, avec troubles marqués de la sensibilité et ataxie des mouvements, et relevant d'une névrite interstitielle hypertrophique à marche ascendante, avec lésions medullaires consécutives." Many of the cases since recorded depart in various particulars from this description. On the pathological side the term interstitial would seem to be misleading, for the characteristic lesion is not so much the increase of interstitial tissue as the hypertrophy of the sheath of Schwann. On the clinical side some writers (e.g., Boveri [1]) have laid particular stress upon the familial incidence and have called the disease "familial hypertrophic neuritis." This departure from the views of Dejerine and Sottas, who did not regard the disease as *essentially* familial, has not been justified by later reports. Cases have been recorded which like our own have begun in adult life, so that if the title is to be inclusive the qualification "de l'enfance" must be abandoned.

In all the cases which we shall review the clinical picture has

been that of a progressive polyneuritis, and hypertrophy of the peripheral nerves, if not definitely recorded during life, has been present post mortem. The title "Progressive Hypertrophic Polyneuritis" appears to us therefore the most suitable.

Clinical Literature.

At the time when Dejerine and Sottas wrote their paper, Charcot and Marie and Tooth had recently described that form of progressive muscular atrophy which bears their joint names. Dejerine and Sottas, in a review of the literature of this disease, emphasized the points of similarity with and difference from that which they were about to describe. Their two patients were a woman of 45 (with post-mortem examination) and a man of 33—brother and sister. The two remaining brothers in the family were unaffected.

Case 1.—In the first case, that of the woman, some difficulty in walking had been observed from childhood, and at the age of 12 she had orthopædic treatment for her deformed feet. Wasting and weakness of the lower limbs were slowly progressive. The upper limbs were involved some years later. She had occasional pains of lightning character in the left thigh. She married at 32 and had one healthy child. On examination, within three years of her death, the following were the outstanding clinical features:—

Muscular atrophy of a peripheral type: both lower limbs below the knees were almost completely paralysed; the thighs were less severely affected; the hands had atrophied but were not completely paralysed; the fore-arms were slightly affected, but the remaining musculature was normal.

Sensory disturbance of a glove and stocking distribution, with loss to light touch up to the level of the upper third of both lower limbs and on both hands; reduction up to groins and axillæ, and blunting of sensibility to pain and temperature, with retarded transmission of sensation, gradually diminishing from the periphery to the root of each limb. The sense of position was impaired in the upper and lower limbs.

The tendon-jerks were all abolished and the plantar responses were absent.

The electrical reactions showed no response to faradism in the legs, thighs and hands, and a sluggish response in the fore-arms. To galvanism a sluggish response was obtained without inversion of formula.

Pupils.—The left eye had been operated upon for cataract. The right pupil was small. The reaction to light was preserved, but extremely slow and often difficult to observe.

Fibrillation was observed at times in the muscles of the limbs and also in the lower part of the face.

The other features recorded were: slight nystagmus on lateral fixation, inco-ordination in voluntary movements of the upper limbs and a marked kypho-

scoliosis. The patient's mentality was somewhat childish. The genito-urinary functions were normal.

No hypertrophy of the peripheral nerves was noted during life.

Case 2.- In their second case kypho-scoliosis was known to have been present since the age of 5. Difficulty in walking was first noticed at 15 and was progressive. About the same time the patient began to suffer with lightning pains, chiefly in the lower limbs but also in the upper limbs. Wasting and weakness of the hands compelled him to give up his work as a printer. His speech became scanning. At the age of 24 he acquired syphilis.

Clinical examination at the age of 30 showed muscular atrophy and sensory disturbance of a type and distribution similar to that already observed in his sister. As in her case, the tendon-jerks were abolished and the plantar responses were absent.

The muscles of the thighs, legs and fore-arms gave no response to faradism. The pupils were small, unequal, irregular in outline and their reactions were of the Argyll-Robertson type. Fibrillation was observed in the muscles of the limbs and of the face. As in the other case, slight nystagmus was present, but was associated in this instance with scanning speech, and with more evident inco-ordination of voluntary movements in the upper limbs. A considerable degree of deafness was present, which had been progressive for some years. Kypho-scoliosis was a marked clinical feature. Mentality was subnormal. The genito-urinary functions were normal.

No hypertrophy of the peripheral nerves was noted until after the discovery of this feature at the autopsy on his sister; the patient was then re-examined with especial attention to this point, and it was observed that all the accessible nerve trunks were increased in volume, of a diameter twice the ordinary, and very hard to palpation.

The résumé of these cases has been made in some detail in order that certain points may be stressed in the conception held by Dejerine and Sottas of the disease which they were the first to describe. The clinical picture is essentially that of a severe progressive polyneuritis with the disturbance of motor, sensory and reflex function which one would expect in such a condition. The hypertrophy of the nerves was by no means a striking feature of either case. In the first it was discovered only post mortem, and in the second only after this post-mortem discovery had led to a particular search for hypertrophy in the nerve trunks of the survivor. The Argyll-Robertson pupils observed in the second case may reasonably be attributed to the syphilitic infection; they must, therefore, be excluded from the clinical picture of the disease under discussion. As regards pupillary signs, therefore, we are left with the single observation on the first case of a small and sluggish pupil. In addition to the clinical picture of a slow progressive polyneuritis, in

itself a rarity, we have the familial incidence, the nystagmus and incoordination, the kypho-scoliosis and the mental retardation.

In their review of the literature Dejerine and Sottas were able to find only one example of the disease, a case reported by Gombault and Mallet [7], in 1889, under the title of tabes.

Case 3.—The patient was a man, aged 58, in whom the disease had apparently commenced when he was 7. There was no family history of the malady. There was flaccid paralysis and atrophy of the whole of both lower limbs, the hands and fore-arms; stocking and glove anaesthesia; loss of tendon-jerks and kypho-scoliosis. He had lost one eye and there is no mention of the pupillary reactions in the other. No note was made of hypertrophy of the nerves during life, but at the post-mortem they were recorded as slightly larger than usual. The nerve roots were found to be grossly hypertrophied, and the histological picture as described and illustrated in their paper is analogous to that of the Dejerine-Sottas case.

Cases 4 *and* 5.—In 1906, Pierre Marie presented two cases from a family of seven who were all said to be suffering from the same malady. The main symptoms were atrophy of the musculature of feet and legs, marked diminution of cutaneous sensibility, especially to touch, absence of the knee and ankle jerks and of the plantar responses, and kypho-scoliosis. The nerve trunks were thickened. Some of the subcutaneous nerves, e.g., the internal cutaneous and superficial cervicals, were unduly prominent. The pupils reacted to light but sluggishly, the speech was scanning, tremor of an intentional type was present, and all members of the family showed a slight exophthalmos.

Boveri [1] in 1910 reported Marie's cases in greater detail, together with a post-mortem report upon one of them which confirmed the pathological diagnosis. In the meantime one of the younger members of the family had developed muscular atrophy of the hands. In three the pupils were small and reacted only sluggishly to light. None had true nystagmus. One only—the eldest—had scanning speech and intentional tremor. All had some degree of sensory disturbance of the polyneuritic type, with absent deep reflexes. All showed some degree of kypho-scoliosis and exophthalmos. None had complained of lightning pains.

Boveri sought to make what appears to us a needless distinction on the basis of minor discrepancies between a Gombault-Dejerine and a Pierre Marie type of the disease, a distinction at once denied by Dejerine [2] but perpetuated by subsequent writers.

Case 6.—At the same time Boveri reported a new case from Marie's service, seen and accepted by him as such on account of the thickening of subcutaneous nerves. In this case, which was somewhat inadequately reported, there was no family history of the disease, the pupils reacted to light normally, but the main features of the disease, including the early onset and the kypho-scoliosis, were as already described. The case had previously been diagnosed as Friedreich's ataxia.

There are, however, two points worth observation in this case, the first that the patient at one stage in his illness lost the use of his hands and subsequently regained it; the second that this is the first instance in the literature in which the diagnosis is recorded without pathological verification, and it was made upon the association of a polyneuritic picture with visible and palpable hypertrophy of the peripheral nerves.

Case 7.—Long [9] in 1912 recorded a case under the title of "Atrophie musculaire progressive Type Aran-Duchenne de Nature névritique," in which there was no apparent hypertrophy of the peripheral nerves during life, nor of the nerves or nerve-roots after death, yet microscopic examination revealed an irregular but widespread hypertrophy of the sheath of Schwann, practically confined to the anterior roots between their emergence from the cord and their junction with the posterior roots. Clinically the case was one of progressive muscular atrophy commencing in the left hand at the age of 53, gradually progressive until death twelve years later, with involvement of all the musculature of the left upper limb, the right hand, and to a less extent the lower limbs: all the tendon-jerks were abolished and the plantar responses were absent. The pupils reacted normally. There were vague pains in the limbs and fibrillary twitchings, but no sensory loss.

Long admits that the absence of sensory loss in this case is a point of clinical distinction from the Dejerine-Sottas cases and other cases of this group reported up to date, but from a comprehensive review of the literature quotes other instances in which cases of progressive muscular atrophy of the "neuritic" or Charcot-Marie type and distribution have shown post-mortem hypertrophy of the sheath of Schwann (Virchow, Friedreich, Dubreuilh, Nonne, Casazza, Aoyama).

Case 8.—Schaller [14] in 1912, recorded a male, aged 20, in whom the clinical diagnosis was made upon the presence of hypertrophy of the nerve trunks of the axilla, the ulnar nerve at the bend of the elbow, the superficial branches of the cervical plexus, and the cutaneous popliteal. One of the enlarged superficial cervical nerves was excised for microscopic examination, and showed changes which are somewhat incompletely described but appear to have been characteristic. The main clinical features were a history of seven years progressive weakness, beginning in the legs and arms without any noticeable atrophy; blunting of cutaneous and deep sensibility of glove and stocking distribution; abolition of all the tendon reflexes except the triceps jerks, and partial R.D. in the weakened muscles. The pupils were normal. There was no family history of the disease, two sisters being alive and well.

Cases 9 *to* 13.—Hoffmann [8] (1912) reported five cases under the title of "Progressive Hypertrophic Neuritis," in which the diagnosis in each instance was based upon diffuse palpable hypertrophy of the peripheral nerves. The details of his third case are those of a polyneuritic picture with peripheral atrophy, sensory loss and absent tendon-jerks in a male of 20, with a progressive history from childhood. The history included tearing pains in the legs

and trunk, and paræsthesiæ of the extremities. This patient's mother (Case 4 of Hoffmann's series), aged 48, showed wasting and deformity of the feet and some wasting of the hand muscles, with absent arm-jerks and ankle-jerks, the knee-jerks being present. There was no sensory disturbance. The ulnar, median and peroneal and tibial nerves were thickened and hard. The history was that of a progressive weakness of the feet of nine years' duration.

These two cases are of particular interest, in that the mixed sensory and motor symptoms in the son were associated with purely motor symptoms in the mother. Here we have a link between the more characteristically polyneuritic form of the disease and that in which the motor functions are chiefly or, in some instances, solely affected. Hoffmann's other three cases were non-familial, began at various ages from 3 to 30, and were distinguished by progressive wasting and weakness of the extremities with occasional bouts of tearing pains and absent tendon-jerks, without paræsthesiæ or sensory loss.

Cases 14 *and* 15.—Yokomori [17] (1915) reported two cases of hypertrophic neuritis in a father and son in whom the disease did not make its appearance until adult life, beginning at the age of 44 in the father, and at 26 in the son. The clinical findings were similar in both cases, though muscular atrophy was more advanced in the case of the father who died at the age of 74, and on whom an autopsy was obtained. The initial symptoms were those of weakness and wasting of the muscles of the legs. The arms were affected much later. In both cases there was much wasting of the distal muscles of the limbs; a talipes equinus; absent knee and ankle jerks; loss of appreciation of pain and temperature below the knees and on the fore-arms and hands, and a palpable, painless thickening of the peripheral nerves, especially of the radial and ulnar. This thickening was confirmed post mortem in the one case when a similar thickening of the brachial and lumbar plexus was found. No nystagmus was observed in either case and the cranial nerves appeared normal.

Case 16.—Dide and Courjon [6] recorded a case in 1918, which was almost simultaneously recorded by Roussy and Cornil [13], having passed from one hospital to another during the war. Roussy and Cornil confirmed the diagnosis by histological examination of a fragment of one of the thickened nerves removed during life. The case is of interest in that it was non-familial; the symptoms began in adult life at the age of 40, commenced in the hands, only later affecting the lower limbs, and at the time of examination four years after the onset the disease was asymmetrical, affecting the left upper and lower limbs more than the right. Kypho-scoliosis was absent; the pupils were normal; there was no nystagmus. Intentional tremor, however, was present. The supinator and ankle-jerks were absent, the triceps-jerks present, the right knee-jerk present but the left feeble. Intermittent shooting pains had been experienced in the lower limbs, but the only sensory disturbance was in the domain of the left ulnar nerve. The spinal fluid showed 5 cells per c.mm., and a positive Wassermann reaction (the W.R. however was reported negative by

Dide and Courjon). Roussy and Cornil regarded the histological appearances in this case as a sufficient warrant of the diagnosis. They refer to Long's case as analogous. They mention also a case recorded by Chiarini and Natzari, which was distinguished by the absence of any sensory disturbance, the case clinically corresponding with the Charcot-Marie-Tooth disease. The diagnosis was determined by pathological examination.

Cases 17 *to* 21.—Dide and Courjon [5] in 1919 reported five new cases. None of these was confirmed by biopsy or autopsy, nor will the clinical details bear critical examination in comparison with the cases already reviewed. In Case 1 there was unilateral ulnar paresis with thickening of the nerve in the olecranon groove; in Case 2 atrophy of the left hand and fore-arm with thickening of median and ulnar nerves, but no sensory loss or abolition of reflexes. In Case 3 atrophy of the intrinsic muscles of the right hand was noted, with thickening of the ulnar nerve. In Case 4 there was atrophy of the upper limbs, with ape-like hands, and also of the small muscles of the feet; no loss of tendon-jerks, no sensory loss, but thickening of the median and ulnar nerves. In Case 5 there was distal wasting of upper and lower limbs, no loss of sensation or reflexes and thickening of median and ulnar nerves. Without pathological verification we feel that none of these can be accepted as an example of progressive hypertrophic polyneuritis.

Case 22.—Nattrass [12] in 1921 reported as a case of recurrent hypertrophic neuritis a boy, aged 18, seen in his third attack. The main clinical features were a subacute onset of polyneuritic symptoms with extensive paralysis, tingling in the extremities without objective sensory loss and abolition of tendon-jerks; recovery was almost complete at the end of three months. The peripheral nerve trunks were hard, enlarged and tender; no enlargement of subcutaneous nerves was observed. No pathological examination was made, and in the absence of such verification this case can hardly be accepted as a true instance of the disease under discussion, for a recurrent toxic or infective polyneuritis might well leave in its wake some thickening and tenderness of the peripheral nerve trunks.

Case 23.—Souques [15] (1926) published the case of a woman, aged 58, in whom the disease appears to have begun in childhood, first affecting the feet and progressing very slowly. At the date of publication there were extreme atrophy and almost complete paralysis of all muscles below the knees and of the muscles of the hands. The thighs were affected but to a lesser degree. The upper limbs apart from the hands were normal. All tendon reflexes and the plantar responses were abolished. Fibrillation was seen in the affected muscles. The paralysed muscles showed no response to faradism, those less affected a partial R.D. There was slight but definite sensory disturbance of peripheral distribution. The pupils were normal, there had been no lightning pains and other subjective sensory disturbance. There were no signs of cerebellar defect and no spinal deformity. The clinical diagnosis was based upon the hypertrophy of the peripheral nerves, both palpable and visible.

Cases 24 *to* 26.—Pathological reports without clinical record were also given by Marie and Bertrand (1918) [11] of two cases, and by Souques and Bertrand (1921) [16] of one case.

Pathological Literature.

The first account of the pathology of familial hypertrophic neuritis was that of Dejerine and Sottas [3] in 1893, who obtained their material from their first published case. The autopsy on the case which Gombault and Mallet [7] had recorded four years previously had revealed a pathological picture similar to that described by Dejerine and Sottas, but Gombault and Mallet insisted in their paper on ascribing the peculiar lesions of the nerves to a sequel of the tabetic process in the spinal cord. If the clinical diagnosis of tabes in this case is questioned there can be no doubt that Gombault and Mallet were the first to describe the pathology of hypertrophic familial neuritis; they, however, failed to recognize it as a new pathological entity.

Since 1893 about nine cases of hypertrophic familial neuritis have come to autopsy of which there are records of the changes in the nervous system. In addition there have been two cases (Schaller [14], and Roussy and Cornil [13]) in which a biopsy has been performed on one of the hypertrophied nerves. The principal pathological findings have, in the main, been remarkably constant, varying only in degree.

The complete extent of the lesions and their significance have not yet, however, been accurately determined. The earlier observers laboured under the disadvantage of restricted technical methods, whilst later workers have seemed to confine their attention to the investigation of lesions by one or two of the most modern methods. For this reason, and also in view of the small number of cases reported pathologically, it appeared worth while to make as complete an examination as possible of our case of progressive hypertrophic polyneuritis.

It is here convenient to summarize the pathological changes hitherto recorded in this disease :—

(1) *The nerves.*—Pathologically the characteristic feature of the disease is the great increase in volume of the peripheral nerves. This increase in volume is greater in some nerves than in others. Marie and Bertrand [11] remarked that whereas the median nerve was relatively thin, the radial was the size of a normal sciatic. Boveri [1] found the diameter of the sciatic nerve 5 cm. below its exit from the pelvis to be 18-19 mm. Some authors have found the cranial nerves

to share in the increase in volume (e.g., Dejerine and Thomas). These authors also found that the cervical sympathetic was greatly hypertrophied.

The microscopical lesions found in the nerves can be divided into those which affect the interstitial tissue and those which are incident upon the nerve fibre itself. The former do not differ essentially from interstitial hypertrophy in other forms of neuritis. Epineurium, perineurium, and endoneurium have all been found increased in amount by various authors, though there has been some difference of opinion as to the relative increase in each of these. Dejerine and Sottas described the interstitial hypertrophy as occurring most in the perineurium: Yokomori [17] confirmed this, but Souques and Bertrand [15], on the other hand, stressed the hypertrophy of the endoneurium. But, as Marie and Bertrand point out, the great increase in volume of the nerves is due in some cases, not to the thickening in the interstitial tissue, but to an increase in tissue derived from the nervous elements.

The characteristic and outstanding lesion described in this disease is the hypertrophy and proliferation of the sheath of Schwann. Gombault and Mallet recognized this, and subsequent workers have confirmed their finding. The changes in the sheath of Schwann vary from simple hypertrophy with increase in nuclei around a single nerve fibre (Yokomori), to extensive proliferation and coalescence into masses, which may contain numbers of axis-cylinders (Marie and Bertrand), or the proliferating sheath may become flattened out into layers which appear imbricated and have been compared to the section of an onion (Dejerine and Thomas [4], Roussy and Cornil [13], Boveri [1], Souques and Bertrand [16].) Marie and Bertrand [11] have described what they consider an intermediate stage between these two extreme forms of proliferation. In the nerves of their cases they found masses of a tissue which was multinucleated and contained many thin unmyelinated axis-cylinders. The fact that these multinucleated masses contained numbers of axis-cylinders was held by Gombault and Mallet, and later by Souques and by Roussy and Cornil, to be evidence that these bare axis-cylinders were attempts at regeneration of the nerve fibres.

Souques and Bertrand differentiate the swelling and proliferation of the sheath of Schwann from that of the interfibrillar connective tissue or sheath of Key and Retzius, which lies outside the sheath of Schwann and in apposition to it, and which is greatly hypertrophied in this disease (Souques and Bertrand, Roussy and Cornil).

In every recorded case the myelin sheaths have been few in number in the peripheral nerves, many fibres being completely devoid of myelin Dejerine and Sottas noticed that this loss of myelin was greater in the distal part of the nerve than in the proximal part. There has been more diversity of opinion about the condition of the axis-cylinders in the peripheral nerves than about any other lesion. Dejerine and Sottas found that most axis-cylinders had disappeared. Souques and Bertrand observed some degeneration of the axis-cylinders with fragmentation, the fragments often ending in an arborization which was strongly argentophil. Marie and Bertrand came to the conclusion that although some axis-cylinders were swollen and others appeared rather thin, they were, in general, well preserved. Yokomori decided that the axis-cylinders were relatively normal in the neighbourhood of the spinal cord, but very scanty peripherally, with occasional swellings in part of their course. They might even disappear completely toward the end of the nerves.

(2) *The nerve roots and cauda equina.*—Gombault and Mallet, Dejerine and Sottas, Souques and Bertrand and Dejerine and Thomas in both their cases described an appreciable macroscopic thickening of the cauda equina, but to Boveri and to Yokomori the cauda equina appeared normal. Neither did these two authors find the nerve roots hypertrophied. The other writers quoted above found a thickening of both anterior and posterior roots. The lesions in the roots were similar to those in the peripheral nerves, but more intense (Marie and Bertrand, Dejerine and Thomas), especially the demyelination (Dejerine and Sottas, Gombault and Mallet), and the formation of "onion bulb" masses (Marie and Bertrand). Dejerine and Sottas found these changes most extensive in the anterior roots of the cauda equina.

(3) *The spinal ganglia.*—The lesions of the spinal ganglia have been studied especially by Marie and Bertrand and Souques and Bertrand.

Marie and Bertrand detected many signs of degeneration in the ganglion cells. In some the nucleus had entirely disappeared, in others the neurofibrils had disappeared from part of the cell body, whilst in others the cell had taken on a pseudo-amœboid form. Around most of the nerve cells there was an increase in satellite corpuscles. No mention is made of the presence of any masses of tissue derived from the sheath of Schwann or capsule cells in the ganglia.

Souques and Bertrand noted changes only in the lumbar and sacral ganglia, the dorsal and cervical appearing normal, though the latter were macroscopically hypertrophied. These authors mention multipli-

cation of the capsular nuclei and hypertrophy of the extracapsular layers of cells. They also describe various stages of degeneration of the ganglion cells, up to the final stage of a mass of amorphous cellular tissue surrounded by satellite corpuscles. The ganglion cells, although most of them showed degenerative changes, were normal in number. Dejerine and Thomas [4] in their second case reported a decrease in the number of ganglion cells, with atrophy of those remaining, and hyaline degeneration of the blood-vessels. Gombault and Mallet observed interstitial changes in the ganglia similar to those occurring in the roots, but normal ganglion cells.

(4) *The spinal cord.*—Degeneration of the posterior columns of the spinal cord has been described in all the recorded cases of this disease, and is considered to be a sequel to the pathological process in the nerves. Dejerine and Sottas first noticed that the degeneration was most severe and extensive in the lumbo-sacral region. In the dorsal and cervical regions the column of Goll only was affected, the column of Burdach escaping. This was confirmed by Dejerine and Thomas, Souques and Bertrand, and Marie and Bertrand, though Boveri and Yokomori found that the degeneration was present only in the inner part of the column of Goll throughout the cord. In Boveri's case the crossed pyramidal tracts, the direct cerebellar and the direct pyramidal tracts also appeared pale when stained by the Weigert-Pal method, but Boveri himself suggested that this apparent degeneration was due to an error in technique.

Marie and Bertrand and Souques and Bertrand traced the degeneration of the posterior columns up as far as the nucleus gracilis in the medulla. No lesions have been discovered above this level. Yokomori has described an increase in neuroglial tissue in the posterior columns of the cord. Other writers make no mention of neuroglial reaction.

There has been some difference of opinion as to the condition of the anterior horn-cells in the spinal cord. Dejerine and Thomas described atrophy of a certain number of them, but considered that most were normal. Boveri also observed atrophy of the cells, but was not completely satisfied with his methods of examination. Yokomori found that they were much diminished in number, whilst those remaining were atrophied, especially in the dorsal region; though the neurofibrils running through them appeared to be thickened. Souques and Bertrand also described a diminution in the number of anterior horn-cells, many of which exhibited all the signs of an acute cytolysis.

(5) *The muscles.*—All observers agree that in muscles atrophied

during life a simple atrophy is found histologically. In addition, Dejerine and Sottas and Dejerine and Thomas noted a thickening of the blood-vessels, whilst Marie and Bertrand interpreted the changes in the blood-vessels as a mesarteritis rather than as an endarteritis or periarteritis. These authors, and also Gombault and Mallet, Boveri, Dejerine and Thomas and Yokomori, reported an increase in interstitial fat in the muscles.

The essential lesions of progressive hypertrophic polyneuritis would therefore appear to be:—

(1) A hypertrophy of the peripheral nerves, ganglia, and spinal roots, depending on two factors—one an increase in the interstitial tissue; the other, which is peculiar to the disease, a proliferation of the cells of the sheath of Schwann, with a concomitant demyelination of nerve-fibres.

(2) An associated degeneration of the posterior columns of the spinal cord, the relation of which to the lesions in the nerves and nerve-roots may be consecutive, though this has not yet been definitely decided.

Clinical History of the Case.

C. H., aged 52, carpenter, was admitted into Guy's Hospital under Dr. J. J. Conybeare, on September 15, 1927. He complained of pains and numbness in his arms and legs, diarrhœa and attacks of faintness with loss of consciousness.

The illness had commenced three years previous to admission, and the first symptoms were pains in the arms, which worried him particularly at night while in bed: and dulness of sensation in the hands, the latter chiefly in the mornings. He next began to lose energy and appetite, and gradually became weaker, so that he was obliged to give up his work. Later he began to suffer with stabbing pains in his legs: these were like exaggerated pins and needles, felt chiefly in the calves and in the soles of his feet. These pains also came on chiefly at night and disturbed his sleep. By about August, 1926, diarrhœa became a troublesome symptom. He would pass on the average two or three watery motions in the twenty-four hours, and sometimes the bowels would act without his being aware of it. He stated that he had suffered from momentary lapses of consciousness, which would come without warning at any time: they would last only a few seconds. On one or two occasions he had fallen, but had never hurt himself. He had never passed urine in any of these attacks. He did not feel dazed after an attack.

He could give no history of any previous illness, except pneumonia as a child, and influenza several times. He had never had syphilis.

Family history.—He was married and had two living healthy children. Two brothers died from complaints similar to his own: he was emphatic that his brothers had suffered in precisely the same manner as himself and that in each case death had taken place three years after the onset of symptoms.

Dr. Charles Ham, who had been the family doctor for many years, very

kindly wrote a letter in reply to inquiry which, in view of the many details which it contains, we quote in full.

"I will be only too glad to give you the history as far as I know it of the varied members of the H. family, and if you find anything further in your investigations, I should be glad if you would let me know.

The father died of tubercle, the mother of old age. One sister died of asthma and tubercle. The diagnosis in these cases was quite definite. One sister, about 55, is alive and fairly well.

The following three (a sister and two brothers, all dead) presented great difficulties in diagnosis and in fact they were not really diagnosed at all.

The sister, whom I saw a short time before she died, was suffering with acute diarrhœa, the heart was dilated, and there was a trace of albumen in the urine. At the time I did not realize the nature of the case, but getting the history after her death from the sister I think she must have suffered in the same way as the brothers.

The symptoms in the two brothers I attended were very similar, and to save time I will describe them together. First, they complained of tiredness in legs and lack of sleep, then shooting pains developed in the legs which were very severe, and symptoms exactly like a peripheral neuritis developed. There was no evidence of alcohol or arsenic, but the teeth were very septic and there was also a marked growth of streptococci in fæces. The urine was quite normal. Nothing else of an abnormal nature was found. The teeth were extracted, but no change in symptoms followed.

The patient gradually got worse, the pain more marked, and the legs became very thin. The heart, lungs, and other organs were apparently healthy. This state of affairs went on for several months: then vomiting set in, and profuse diarrhœa—very offensive and with practically no control: both these symptoms continued on and off right to the end. Other symptoms were emaciation, frequent attacks of unconsciousness lasting from one to four or five minutes, great depression, great distaste for food and very little saliva. The legs remained the same—often a great deal of pain. Towards the end the heart became dilated and a trace of albumen appeared in the urine. X-rays showed nothing.

Both brothers had absence of acid in stomach contents. The fæces gave an abundant growth of Gaertner's bacillus. One brother had signs of pancreatic deficiency.

I understand a post-mortem examination was done on the patient who died in King's College Hospital. They told me nothing was found abnormal except a little fluid in the chest.

I could not get an autopsy on the second brother."

Dr. C. E. Newman, of King's College Hospital, kindly furnished the

following extract from the notes on the case of the youngest brother, who died in that hospital at the age of 52 :—

> "E. H. was in this hospital from 29.12.22 to 16.1.23. He had chronic colitis and neurasthenic symptoms, but with a true peripheral neuritis in the legs. There was excess of streptococci in the fæces. He died suddenly of œdema of the lungs. At the post-mortem examination the heart was absolutely normal, the lungs were œdematous but the changes were acute only. The brain was normal. There were patches of degeneration and replacement fibrosis in the zona fasciculata of the suprarenals and of the sympathetic ganglia: also patches of replacement fibrosis in the femoral and external popliteal nerves. He had œdema and trophic changes in the skin of both feet."

Condition on admission.—The patient looked wasted, particularly in the lower extremities. He had been bedridden for some months and was unable to stand upright without support. In describing his condition he explained that the legs and feet were anæsthetic to light touch, heat and cold, but at the same time he suffered with burning pains on the soles of his feet.

Cardiovascular symptoms: The apex beat could not be felt; the heart sounds were extremely feeble, but no murmurs were heard. Systolic blood-pressure was 95 mm., diastolic 60 mm., hæmoglobin 72 per cent., white cells 9,500 per c.mm., red cells 4,200,000 per c.mm. The differential count normal. The blood Wassermann was negative.

Alimentary system: His tongue moist and clean. All teeth had been extracted some years before for pyorrhœa alveolaris. No pigmentation was present in the mouth. The liver and spleen were not palpable.

Chemical examination of fæces: "Acid to litmus; slight excess of fatty crystals; some fat globules and striated meat fibres. No lack of stercobilin. No hæmatoporphyrin; guaiac negative."

Bacteriological examination of fæces: "Cultures gave a mixed growth of *Bacillus coli communis* and *B. lactis aerogenes*.

Fractional test meal: Marked hypochlorhydria with some free hydrochloric acid at the end of two hours.

An alimentary X-ray showed no abnormality. The urine was normal, and there was no disturbance in the respiratory system.

Central nervous system: Intelligence was normal and he appeared to have a good memory. There was no speech defect. The visual fields were normal and the optic discs showed no abnormality.

A watch was heard at 3 ft. on either side. The pupils were small and the right was a little irregular in outline. Both reacted in accommodation but the reaction to light was sluggish, particularly of the right. The ocular movements were full and normal, and there was no nystagmus. The functions of the remaining cranial nerves were unaffected.

Sensation was normal on the head, palate, trunk and upper extremities. On the lower limbs there was loss of tactile discrimination below the knees.

Sensibility to pinprick was diminished over both legs to about 3 in. above the knees. To cotton wool he was anæsthetic over the feet and on the front of the legs. He was unable to distinguish between heat and cold on the feet and legs. Deep pressure on the muscles caused some discomfort. Vibration

FIGS. 1 and 2.—Hands of patient C. H., showing wasting of intrinsic muscles.

sense was within normal limits, and the sense of position in the joints was not impaired except in the big toes. He was unsteady in the Romberg attitude, but his legs were so weak that they could scarcely support the weight of his body.

There was marked general muscular wasting, but the following groups were especially affected: The intrinsic muscles of the hands, including the thenar

and hypothenar eminences; the flexors of the wrist and fingers, especially on the left: the quadriceps femoris, anterior tibials and intrinsic muscles of the feet. The hand grips were weak. The other muscles of upper limbs and the musculature of the trunk were relatively normal. The extensors of the knees were weak and he was unable to stand unsupported. Dorsiflexion and plantar flexion at the ankles were feeble. There was no power of voluntary movement in the toes. Coarse fibrillary twitching was occasionally observed in the quadriceps of both sides.

FIG. 3.—Lower limbs of patient C. H. showing generalized muscular wasting especially below the knees. The left foot is passively supported.

The electrical reactions of the leg muscles were poor in quality owing to wasting, and there was partial reaction of degeneration as they responded to faradism and gave a slow response to galvanism. The thigh muscles gave better contractions and the reactions were normal, i.e., good response to faradism and brisk contractions with galvanism. The muscles of the upper limbs were not tested.

Some of the peripheral nerves, viz., the ulnars, anterior crurals and external popliteals, were easily palpable but not tender. Above the left clavicle there was some abnormal fulness due to the thickened cords of the brachial plexus.

X-ray examination showed that there was no cervical rib present.

Pathological Examination.

The case came to autopsy on December 1, 1927. There was found considerable atrophy of the muscles of all four limbs, more noticeable distally than centrally.

All the accessible peripheral nerves could be easily palpated. On dissection all the nerves were somewhat larger than normal, but their chief abnormality lay in their excessive firmness. The enlargement of the nerve-trunks seemed to be rather greater close to the ganglia, and there was little diminution in size as one passed peripherally from the ganglia. The nerves proximal to the ganglia did not appear to be much enlarged. The ganglia, on the other hand, were greatly increased in size in the cervical, upper dorsal and lumbo-sacral regions. The upper level of the enlargement of the ganglia was at the sixth cervical, the fifth cervical being small on both sides. There was a distinct difference between the size of the ganglia on the two sides in the cervical and upper dorsal region, the eighth cervical and first dorsal being very much larger on the left than on the right side.

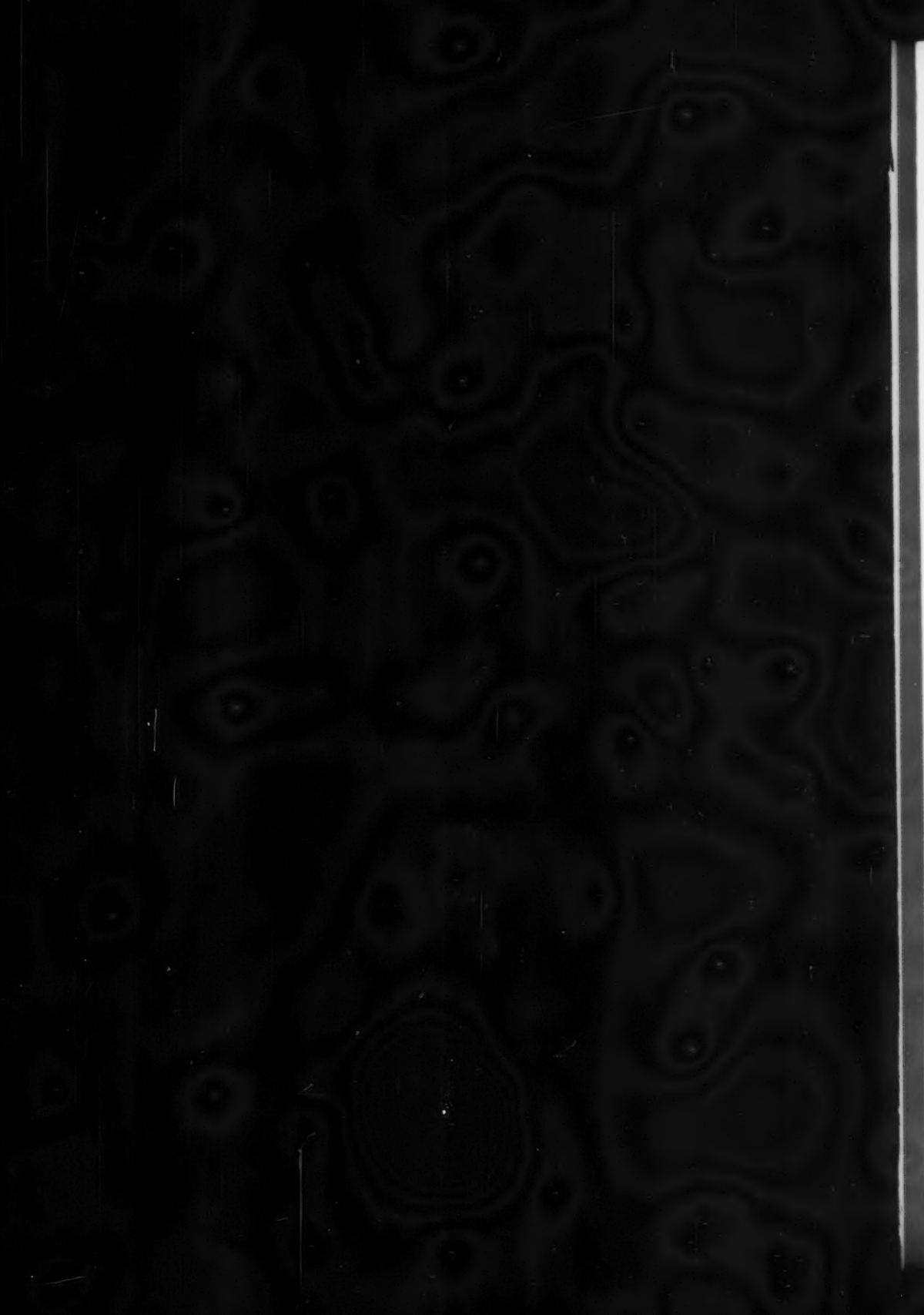
On cross-section of the peripheral nerves it was impossible to see the individual fibres. The nerve appeared homogeneous and resembled a tendon.

Exact measurements of two nerves were made: The musculo-spiral nerve at a distance of 20 cm. from the cord measured 8 by 4 mm. The median nerve at the same distance measured 6 by 4 mm. The diameter of the sciatic nerve throughout its extent appeared to be at least twice the normal. The cranial nerves did not seem to be increased in size. The cauda equina, however, was considerably thickened.

Microscopical Examination.

The peripheral nerves.—Sections of the brachial plexus and of the musculo-spiral, ulnar, and internal cutaneous nerves of the arm were taken at definite measured distances from the spinal cord, 15 and 35 cm. in the case of the nerves of the arm. The sciatic nerve was sectioned in the gluteal region, in the thigh and in the popliteal space. The staining methods employed were those of Weigert-Pal with carmine counterstain, Bielschowsky, Mallory's anilin blue-orange G. (modified), Scharlach R., and iron hæmatoxylin with van Gieson's counterstain and the same stain with an eosin counterstain. The same methods were used for staining the spinal ganglia.

It was in sections stained with hæmatoxylin and van Gieson's counterstain that the characteristic lesion was seen most clearly. Nearly all the nerve-fibres appeared swollen and had an excess of nuclei. In between the nerve-fibres and separating them from one another lay masses of a non-nucleated, homogeneous substance which stained deep yellow with the van Gieson counterstain. These masses for the most part lay irregularly distributed in the nerve-bundle, but in some nerves, especially in the most distal portion of the sciatic they seemed to be collected in a more regular fashion as a layer directly under the capsule of the nerve-bundle. As regards the distribution of these masses in the various portions of the nerves examined, we found that they were more



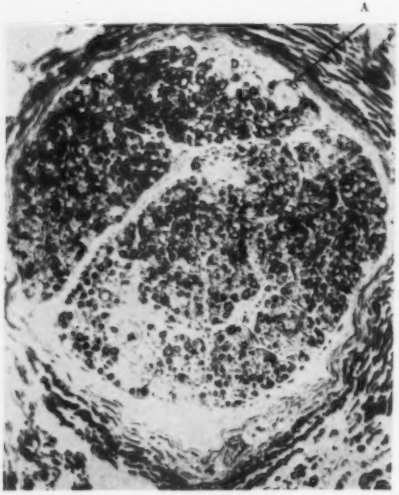


FIG. 4.—Transverse section of median nerve stained by the Weigert-Pal method showing a plasmatic swelling directly under the capsule of the nerve bundle, A. Some nerve fibres appear swollen. There are some demyelinated fibres present, but myelination is relatively good as the section was taken from a high level in the nerve. The interstitial tissue is increased.

FIG. 5.—Transverse section of sciatic nerve stained with hæmatoxylin and van Gieson. The shape of the nerve bundle is grossly irregular and there is much interstitial fibrosis. There are many plasmatic swellings present, some rounded and some irregular in shape. They tend to be collected around the periphery under the capsule, although some are irregularly distributed in the interior of the bundle.

FIG. 6.—Transverse section of cauda equina stained by the Weigert-Pal method. Two large plasmatic swellings are to be seen in the middle of the field, A. Many nerve fibres in one half of the field are poorly myelinated.

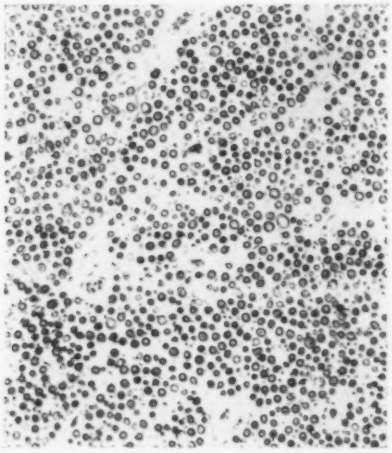


FIG. 7.—Transverse section of cauda equina at a higher level than Fig. 3, stained by the Weigert-Pal method. The nerve fibres are more widely separated than normal by fibrous tissue and there is much thickening around blood-vessels. Some nerve fibres appear swollen.

To illustrate Dr. R. S. de Bruyn's and Dr. Ruby O. Stern's paper.

numerous in the proximal portions of the nerves, whereas degeneration of myelin was more evident in the distal portions. The origin of these masses would seem to be an hypertrophy of the sheaths of Schwann, although no definite intermediate stages between the swollen sheath around a single nerve-fibre and these non-nucleated masses could be determined. We can only assume that these masses are formed of swollen sheaths of Schwann which have coalesced and in which the axis-cylinders, myelin sheaths and nuclei have all degenerated, since we could nowhere find traces of degenerating nuclei, myelin sheaths or axis-cylinders in the masses. Very occasionally a thin axis-cylinder might be seen in the periphery of a mass, but not more often than was a blood-vessel. Boveri described similar masses of a homogeneous tissue, which stained deep red with eosin, in the peripheral nerves. The masses which we have found also stained red with eosin and would appear to be identical with those observed by Boveri. He gave no opinion as to their origin. Careful search for the "onion bulb," laminated masses regarded by the majority of writers as the characteristic lesion in the peripheral nerves failed to reveal them. Nowhere could we find any suggestion of either a laminated or a nucleated mass. We have felt it necessary to give a name to the homogeneous tissue which we have found present constantly in the peripheral nerves, and also, as will be seen later, in the ganglia. To obviate any possible objections to the use of a descriptive term, assuming the tissue to have a certain mode of origin, we propose to call the substance of which the masses are composed "plasmatic substance," which is descriptive only in that it assumes the mass to contain protoplasm. We have called the masses of tissue "plasmatic swellings."

Bielschowsky preparations demonstrated these plasmatic swellings well. They appeared somewhat argentophil, though not so strongly as the axis-cylinders, none of which could be seen to enter the swellings. Axis-cylinders were either pushed to one side and ran around the plasmatic swellings, or they became broken off at the edge of the swellings, where they formed small, terminal, strongly argentophil bulbs. Apart from these interruptions the axis-cylinders seemed relatively normal. They were certainly not increased in number. In a few fibres they appeared rather thin and occasionally small bulbous swellings could be seen on them. The Bielschowsky method also showed very plainly the hypertrophy of the interfibrillar reticular tissue or sheath of Key and Retzius. The wavy fibres of this sheath could be seen surrounding the plasmatic swellings, but never transversing them. These fibres were sometimes a little difficult to distinguish from the axis-cylinders, though usually the latter were easily distinguished by their straighter course and thicker diameter.

In sections stained by the Weigert-Pal method the plasmatic swellings appeared as colourless areas which did not take the carmine counterstain, and in which no trace of myelinated material could be made out. Many fibres were seen to have lost their myelin sheaths and, as we have previously mentioned, this was particularly evident in the distal portions of the nerves.

In the median nerve, for example, at a distance of 15 cm. from the spinal cord myelination was almost normal, but 35 cm. from the cord a large number of demyelinated fibres were present.

In Scharlach R. preparations the plasmatic swellings did not stain, but in several of them minute droplets of orange-red, fat-staining material were to be seen. No droplets of fat could be seen in the nerve fibres.

By the anilin blue-orange G. method the plasmatic swellings stained a deep blue, quite distinct from the paler blue of the interstitial collagenous tissue.

Changes in the interstitial tissue were seen to the greatest extent in the sciatic nerve. In this nerve all the connective tissue coats of the nerve-fibre were greatly thickened, but the perineurium appeared to be the most affected. The chief thickening of the whole nerve was, in the sciatic, due not to the presence of the plasmatic swellings, although numbers of these were present, but to the large amount of interstitial tissue between the nerve bundles. The nerve bundles themselves were grossly irregular in shape. This irregularity was probably caused partly by the shrinkage of the nerve bundles and partly by the irregular distribution of the interstitial tissue. The blood-vessels in the nerves were thicker than normal, the adventitia especially being hypertrophied.

The spinal ganglia.—Sections were taken from the lower cervical and upper dorsal ganglia, and from the fifth lumbar and first sacral ganglia. Similar lesions to those in the peripheral nerves were found in the ganglia, although the interstitial changes were not so intense. Plasmatic swellings were found in all the ganglia. They occurred in two distinct positions: (1) in between the nerve fibres, where they could be seen forming globular or oval masses resembling those in the peripheral nerves; and (2) in relation to the ganglion cells. Here they appeared to arise within the capsule cell layer, and various stages in their formation from these cells could be made out. The earliest stage seemed to be a swelling of the capsule cells with multiplication of their nuclei. In a large number of cells the process was arrested at this stage and the condition therefore approximated to that described by Souques and Bertrand. In other cells, however, the cells became more swollen, and in their cytoplasm there appeared a mass of homogeneous material, staining deep yellow with van Gieson, which was identical with the plasmatic substance. The nuclei disappeared at this stage, and in the next stage the cells became so distended that their walls collapsed and adjacent cells coalesced, forming a large plasmatic swelling. These swellings often indented the external limiting membrane of the ganglion cells, but could nowhere be observed to penetrate into the ganglion cells, although the cytoplasm of these cells appeared distorted as if pressed upon by the plasmatic swelling.

We were able to confirm the degenerative changes in the ganglion cells that have been so frequently recorded. Some cells had undergone such extreme atrophy that they were distinguished from adjacent plasmatic swellings only by their staining reactions with van Gieson's counterstain, or with the

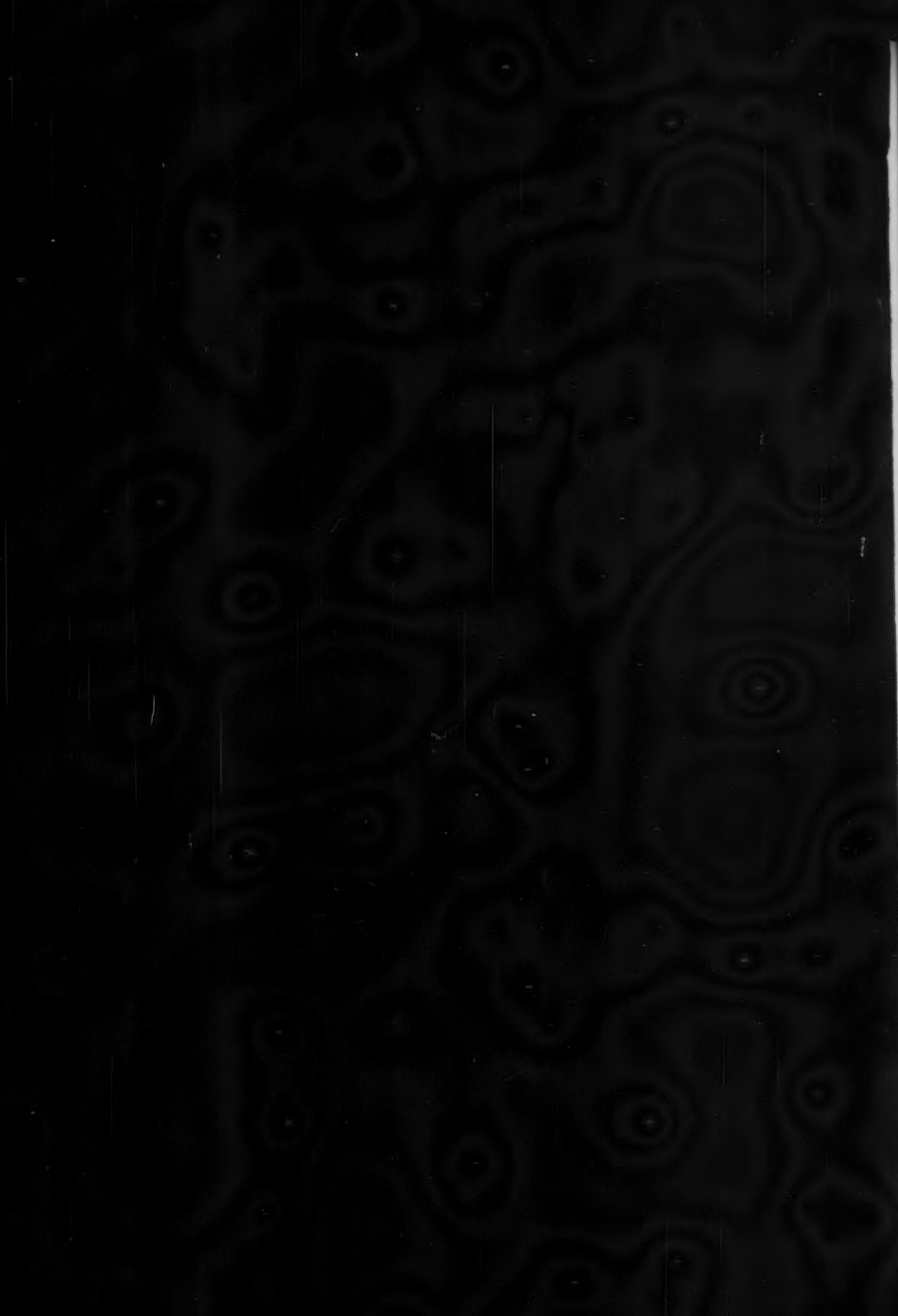


FIG. 8.—Longitudinal section of the left first dorsal root ganglion stained with hæmatoxylin and van Gieson, showing plasmatic swellings among the nerve fibres resembling those in the peripheral nerves.

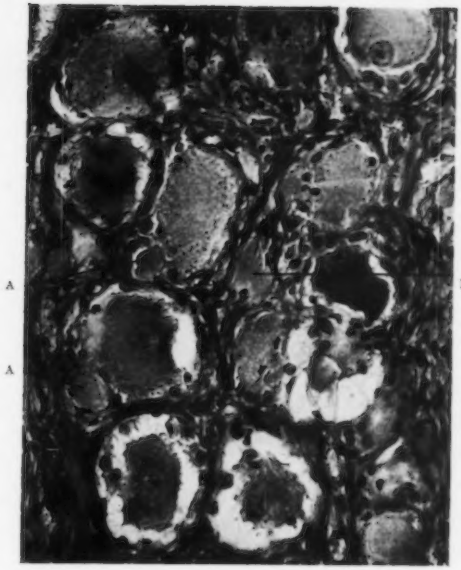


FIG. 9.—Longitudinal section of the right first dorsal ganglion stained with hæmatoxylin and van Gieson. Several rounded plasmatic swellings are to be seen in relation to the ganglion cells A, and others are present in between the nerve fibres B. Most of the ganglion cells are distorted in shape and have eccentric nuclei, and many are shrunken away from their capsules.

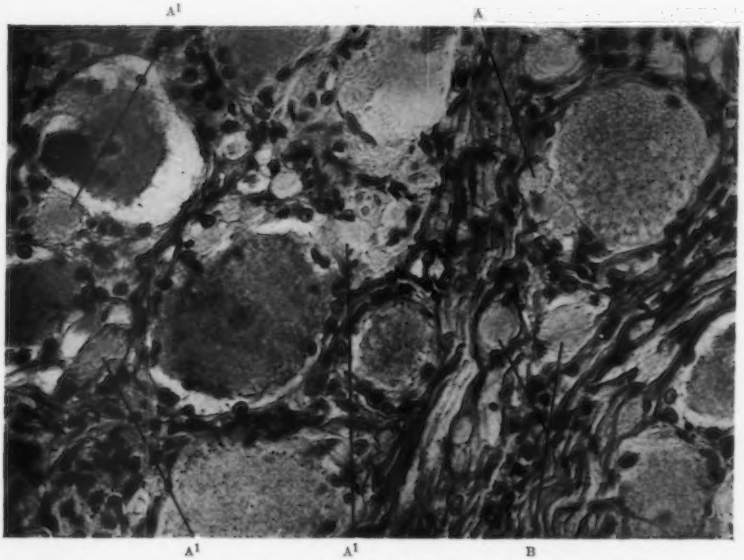


FIG. 10.—Longitudinal section of the right first dorsal ganglion stained with hæmatoxylin and van Gieson, showing plasmatic swellings in relation to the ganglion cells. Three adjacent swellings are to be seen arising in the capsule cell layer of one ganglion cell A. There is hypertrophy of the capsular cells of other ganglion cells with plasmatic swellings A^1 in relation to them and an increase in the amount of interstitial tissue. One ganglion cell containing an excess of melanin pigment has become shrunken away from the capsule cell layer. Some plasmatic swellings between nerve fibres are also seen, B.

anilin blue-orange G. stain. Others showed slighter degrees of degeneration. Many cells were seen with irregular outlines, and in several the external membrane had become infolded. Eccentric nuclei and distorted nuclear shapes were amongst the commoner signs of degeneration observed. In addition, many cells contained an excess of melanin pigment in their cytoplasm. This was noted especially in the first dorsal ganglion. There was an increase in the number of capsule cells around most of the ganglion cells, and in the first sacral ganglion the interstitial tissue was also increased. Myelination was good in the ganglia on the whole, though in each ganglion a few demyelinated fibres could be seen, the position of which was quite independent of the plasmatic swellings.

Nerve roots and cauda equina.—The majority of nerve roots were well myelinated. In a few, the early formation of a plasmatic swelling could be made out as a small, non-nucleated, homogeneous mass which gave the characteristic staining reactions of the plasmatic swellings, lying in between the nerve fibres. The nerve fibres themselves were somewhat swollen, but appeared relatively normal compared with the fibres of the peripheral nerves. There was a slight increase in the interstitial tissue.

The cauda equina showed much more extensive lesions than the other nerve roots. The interstitial fibrosis was particularly striking in some of the bundles of fibres, whilst a large number of fibres were devoid of myelin. There was a copious formation of plasmatic substance, which, even more than in the peripheral nerves, tended to be distributed just under the capsule of the nerve bundles.

Spinal cord.—Only in the sacro-coccygeal region could any very definite degeneration of the posterior columns be found. Otherwise, throughout the cord the posterior columns appear only slightly, if at all, paler than the other tracts when stained by the Weigert-Pal method. In sections stained by the Nissl method the anterior horn cells were for the most part normal in number, size and shape, but in the cervical and lumbo-sacral enlargements a few cells in the lateral group displayed signs of central chromatolysis with eccentric nuclei. As these lateral columns of cells supply the long nerves to the limbs, the affected cells probably corresponded to the nerve fibres in which degenerative changes were most evident.

Bielschowsky preparations showed that the neurofibrils passing through the cells were normal. No cellular infiltration of the cord and no excess of neuroglial tissue could be determined.

Sections of the medulla, pons, mid-brain and cerebral cortex all appeared normal.

Muscles.—Portions of the biceps brachialis and gastrocnemius were embedded in celloidin, stained by iron hæmatoxylin and counterstained with van Gieson. In sections of muscle stained in this way the picture was one of irregular atrophy. Most muscle fibres were of fair size, but very small fibres were also present. The largest observed measured just over 80 μ, the smallest having only their bare nuclei visible. The majority of the fibres were rounded, whilst

a few contained vacuoles in their cytoplasm. No fat replacement or other interstitial change was noted, and the condition was obviously one of "simple atrophy," due to nerve lesion. The vessels were slightly thickened. The nerves in the muscles proved of interest, as in between the nerve fibres were to be seen masses of tissue giving similar staining reactions to, and resembling in their structure, the plasmatic swellings in the peripheral nerves. They were usually found under the capsule of the nerve bundle and in some instances they appeared to be centred on a blood-vessel. Most of the nerve fibres were poorly myelinated as though affected by a lesion at a higher level in the nerve.

Discussion.

Clinically, the case we have recorded corresponds pretty nearly with the original description of Dejerine and Sottas. Our patient, as theirs, presented a polyneuritic symptom picture with wasting, weakness, and sensory loss of peripheral distribution. In both, the pupils were small and reacted sluggishly to light (the Argyll-Robertson pupils observed in their second case must be disregarded for the reasons already given). Coarse fibrillation and partial R.D. were common to both. In both a history of lancinating pains was obtained. In both a striking family history of the disease was present. Certain features present in the Dejerine-Sottas cases, namely kypho-scoliosis, nystagmus and incoordination of the upper limbs, were absent in our own. On the other hand, the history of the disease in our patient differs in the most striking manner from that of the Dejerine-Sottas cases and from all others since described. Our patient died within three years of the onset of his malady, as did his two brothers and one sister who appear also to have been affected by it. Severe diarrhœa was an early and persistent symptom in all the cases of this family; in our case the test meal showed marked hypochlorhydria, and in the other members of the family also there appears to have been a deficiency of acid in the gastric juice.

On the pathological side this case conforms in some respects to those which have already been described. The hypertrophy of the peripheral nerves, due in part to thickening of the interstitial tissue, and in part to the new formation of masses of tissue derived from the sheath of Schwann, the amount of demyelination in the nerve fibres and the changes in the cells of the spinal ganglia resemble the classical pathological picture. But there are several points of difference in our case. The presence of masses of non-nucleated tissue, however derived, in relation to the capsule cells of the ganglia, has not hitherto been recorded; neither could we find any reference to the condition of the nerve fibres in the muscles. Apart from these additions to the histological

study of the disease, there are certain differences in our observations which seem to point to the fact that this case may have been of a slightly different pathological type from those previously described. The complete absence of the "onion bulb" masses in the peripheral nerves, which other writers have considered a characteristic feature of the disease, and their replacement by definite non-nucleated, homogeneous masses, varying in size, and derived apparently from hypertrophied cells of the sheath of Schwann, would suggest that in our case either a slightly different process affected the peripheral nervous system, or that we have observed a different stage in the same morbid process.

The absence of any marked degeneration in the dorsal columns may be due to the relatively short history of the case and to the early nature of the disease in the dorsal nerve roots and ganglia. At the same time the absence of "onion bulb" formations and the curious plasmatic swellings found in the nerves seem to constitute qualitative differences between the pathological process in this case and that found in the majority of cases previously recorded.

Summary and Conclusions.

(1) The original paper in which Dejerine and Sottas reported two cases of the disease, which they were the first to name hypertrophic neuritis, has been summarized in some detail.

(2) These two cases were brother and sister, but in view of an isolated case already reported by Gombault and Mallet (under the title of tabes) Dejerine and Sottas did not regard the malady as essentially familial.

(3) The clinical picture described in the cases of Dejerine and Sottas was that of a slowly progressive polyneuritis with both motor and sensory symptoms.

(4) The pupils were small in both their cases. In one case they were Argyll-Robertson. This patient, however, was known to have had syphilis six years previously. This point, which appears to have escaped the notice of most subsequent writers on the subject, is of particular significance since this is the only case we can discover in the literature in which the Argyll-Robertson pupil was observed. The miosis observed in this and other cases, including our own, is almost certainly due to an extension of the disease to the cervical sympathetic fibres in the first thoracic roots.

(5) In Dejerine and Sottas' first case no hypertrophy of the peripheral nerves or nerve trunks was noted during life. When this was

discovered post-mortem the surviving patient was re-examined with especial attention to the point, and it was noted for the first time that all the palpable nerves were increased in volume.

(6) Thus of two signs which have come to be regarded in some of the modern textbooks as characteristic of the malady, one, the Argyll-Robertson pupil, is shown to have no value; the other, hypertrophy of the accessible nerves, may be inconspicuous, and may be observed only if especially looked for.

(7) A critical review of the cases subsequently reported, based primarily upon those in which the diagnosis has been confirmed by pathological examination, shows that the polyneuritic picture may vary in type and distribution. Thus the upper or lower limbs may be in different cases more, or less, severely affected, and whilst as a rule sensory and motor symptoms develop *pari passu*, the one group may precede or overshadow the other.

(8) In addition to the polyneuritic signs, certain others, such as kyphosis, nystagmus and motor inco-ordination, were observed by Dejerine and Sottas in their two original cases and are recorded in a certain number of those subsequently reported.

(9) The age of onset in nine of the fourteen cases in which this point was ascertained was under 21 years. In the remaining five the disease began at the ages of 26, 39, 40, 44 and 50.

(10) A familial history is recorded in four pairs of cases out of a total number of seventeen cases which we have accepted as genuine examples of the disease.

(11) The course of the disease has in all cases previously recorded been slowly progressive, and death has occurred from intercurrent disease.

(12) The case which we record is that of a male whose symptoms began at the age of 49. The polyneuritic symptoms progressed rapidly and were associated with severe and intractable diarrhœa. The patient died three years after the onset of his illness. From the information given by the family physician it appears that one sister and two brothers of the patient died with a similar disease.

(13) The outstanding clinical features of the case were the signs of a severe polyneuritis, both motor and sensory, with major involvement of the lower limbs. The pupils were small but reacted sluggishly to light. The cords of the brachial plexus and the peripheral nerves were easily palpable and thought by some observers to be thickened.

(14) The pathological changes were mainly incident upon the peri-

pheral nerves and spinal ganglia. The degeneration of the posterior columns of the spinal cord described in every case hitherto reported, was almost completely absent in our case. In the peripheral nerves both interstitial and neural elements were hypertrophied. In the distal portions of the nerves there was much loss of myelin.

(15) The characteristic feature of the disease process in the nerves was the presence of masses of non-nucleated tissue which appeared to arise from the sheath of Schwann and, fusing, formed larger masses.

(16) Earlier stages in the formation of these masses were seen in the spinal ganglia both in relation to the capsules of the ganglion cells and to the nerve fibres, and also in the fine intramuscular nerves.

(17) The appearance of these non-nucleated masses does not correspond with any pathological appearances in the peripheral nerves hitherto described in this disease and may represent an earlier stage or possibly a slightly different process.

We wish to acknowledge our indebtedness to Dr. J. J. Conybeare for permission to publish the case and enabling us to obtain the post-mortem examination; to Dr. C. P. Symonds, who suggested the true diagnosis at the bedside and has helped us in reviewing the clinical literature; to Mr. J. W. Shackle for a translation of Hoffmann's paper; also to Dr. Charles E. Ham, for providing us with the family history, and to Dr. C. E. Newman for notes of the brother who was a patient in King's College Hospital.

To Dr. J. Godwin Greenfield we wish to express our gratitude for his interest in the pathological investigation of the case and for his valuable advice on the interpretation of the pathological findings.

REFERENCES.

[1] Boveri, P. *Semaine Méd.*, 1910, **30**, 145.
[2] Dejerine, J. *Rev. Neurol.*, 1906, **14**, 558.
[3] Dejerine, J., et Sottas, J. *Comp. rend. de la Soc. de Biol.*, 1893, **5**, 63.
[4] Dejerine, J., et Thomas, A. *Nouv. Icon. de la Salpêtr.*, 1906, **19**, 477.
[5] Dide, M., et Courjon, R. *Rev. Neurol.*, 1919, **35**, 825.
[6] *Idem., idem. Nouv. Icon. de la Salpêtr.*, 1916-1918, **28**, 377.
[7] Gombault, A., et Mallet. *Arch. de Méd. Expér.*, 1889, **1**, 385.
[8] Hoffmann, J. *Zeitschr. f. Nervenheilk.*, 1912, **44**, 65.
[9] Long, Ed. *Nouv. Icon. de la Salpêtr.*, 1912, **25**, 281.
[10] Marie, P. *Rev. Neurol.*, 1906, **14**, 557.
[11] Marie, P., et Bertrand, I. *Ann. de Méd.*, 1918, **5**, 209.
[12] Nattrass, F. J. *Journ. Neurol. and Psychopathol.*, 1921, **2**, 159.
[13] Roussy, G., et Cornil, L. *Ann. de Méd.*, 1919, **6**, 296.
[14] Schaller, W. F. *Arch. Int. Med.*, 1912, **10**, 399.
[15] Souques, A. *Ann. de Méd.*, 1926, **19**, 484.
[16] Souques, A., et Bertrand, I. *Ibid.*, 1921, **9**, 305.
[17] Yokomori, K. *Mitt. a. d. Med. Fak. de K. Univ. z. Tokyo*, 1915. **15**, 1.

A CASE OF RELAPSING INTERSTITIAL HYPERTROPHIC POLYNEURITIS.

BY WILFRED HARRIS, M.D.,

AND

WILFRID D. NEWCOMB, M.B. (CANTAB.).

(From the Wards and Pathological Department of St. Mary's Hospital, London.)

SOME of the pathological specimens of the case on which this paper is based were shown three years ago at the Pathological Meeting of the Neurological Section of the Royal Society of Medicine, on May 13, 1926. The opportunity is now taken of publishing the case at the same time as Dr. de Bruyn and Dr. Stern's somewhat similar case, a point of considerable advantage to those interested in studying the subject. As these authors are dealing fully with the literature, we have avoided unnecessary reference to previously published cases.

Clinically, our case may be said to have resembled a relapsing or recurrent polyneuritis, which was the diagnosis made during life, as the man was well nourished, with big limbs, and no observation of the nerve-trunks being enlarged was made during life. Indeed, the great size of the nerve-trunks and of the spinal roots was a surprise to us at the autopsy, the sciatic nerve being so large, 1½ in. in diameter, that when, six days after death, it was shown at the pathological meeting, a pathologist of experience humorously suggested that we had brought down a bullock's sciatic nerve in place of a human specimen. A photograph of the nerve, cut at the level of the lower border of the gluteus maximus, placed beside a corresponding portion of the sciatic of another man who was rather larger than our patient (fig. 1), illustrates well its great increase in size, even though it had shrunk considerably owing to fixation.

Although the pathological specimens of the nerves in our case resemble both macroscopically and microscopically those originally described by Dejerine and Sottas, and by Dejerine and Thomas thirteen years later, yet clinically our case differs greatly from these. Their cases were familial: a brother and sister who were affected by the disease in childhood had clawed hands and feet, kyphoscoliosis, Argyll-Robertson

pupils and suffered with ataxy and severe shooting pains. Gombault and Mallet's case, published in 1889, was diagnosed as one of juvenile tabes, but resembled those of Dejerine and Sottas. Marie's case also had kyphoscoliosis and partial loss of the pupillary reactions to light, but ataxy and shooting pains were absent. These cases might easily be mistaken for juvenile tabes, and have to be distinguished from Friedreich's disease and from the Charcot-Marie-Tooth type of amyotrophy. Roussy's case, published in 1919, more nearly resembles our case in the age of his patient, 44, the absence of deformities, and the normal pupillary reactions.

Our case, however, differs from all those hitherto published with necropsy, in that the chief clinical feature was recurrent attacks of paralysis resembling polyneuritis during six years, with complete recovery between the attacks of paralysis. His last attack of weakness was progressive for twelve months, with muscular wasting and foot-drop, and at the end there occurred attacks of choking, severe dyspnœa, and finally paralysis of the diaphragm, possibly due to the marked degeneration found later in the roots of the vagus and phrenic nerves. In 1897 Sorgo described a case of recurrent polyneuritis in a man of 50, in which a fatal result followed three attacks of paralysis at intervals of a few months, death resulting from involvement of the respiratory nerves and paralysis of the diaphragm. Obstinate constipation was a feature of the case. Extensive disease of the vessels was found in the muscles, peripheral nerves and cord, due chiefly to thickening of the middle coat with narrowing of the lumina. There was no lesion of ganglion cells, but degenerative atrophy of the muscles and nerves. The man had suffered from syphilis many years before, and the vascular changes were attributed to this; Sorgo noted that the symptoms were much more severe than could be accounted for by the microscopical findings, and he assumed widespread dynamic change in the cells of the central nervous system. His case showed no hypertrophy of the nerves and the pathological changes are entirely different to those in our case, the resemblance between them being limited to the recurrent attacks of polyneuritis and a fatal termination with respiratory paralysis.

Nattrass has described a case with three attacks of polyneuritis at intervals of several years, in which the nerve trunks appeared to be palpably enlarged during life; his patient recovered.

D. K., aged 52, a seaman in H.M. Navy, served during the War in a destroyer in the North Sea, being in perfect health. In 1919, when aged 45, he was demobilized, and soon afterwards he had a "nervous breakdown," complaining

of weakness of the legs with unsteadiness of gait, especially in the dark, and of tingling and loss of sensation in the tips of his fingers. These symptoms cleared up after several weeks, but he had later had four similar attacks, with complete recovery in the intervals. In March, 1925, similar symptoms again gradually developed, followed by weakness of the feet and hands, and a sensation of pins and needles in the hands and feet. He began to find difficulty in distinguishing coins in his pocket and to drop things, and the muscles of the hands began to waste. His arms became so weak that he could not raise them at the shoulders, and the muscles of the legs wasted and the feet became dropped. There was never any pain, nor any weakness of the sphincters. On applying to the Navy Board for a pension on account of his bad health, he was refused on the ground that he was suffering from progressive muscular atrophy, which was unconnected with his service in the Navy. During February, 1926, he improved slightly in his general strength, though he had several slight attacks of choking. These attacks are of interest in view of the severe attacks of dyspnœa and choking which developed in the last few days of his life. There was no history of any similar disease in other members of his family.

One of us was asked to see him on April 4, 1926, and he was admitted to St. Mary's Hospital on April 14. He then had a steppage gait, with complete bilateral foot-drop, and also considerable weakness of the gastrocnemii and of the flexors of the toes. Flexion and extension of the hips and knees were only slightly weakened. The abdominal and trunk muscles were fair. In his arms the deltoids were weak, so that the arms could not be completely abducted at the shoulder, and flexion of the forearms was also feeble. The supinator longus was thin and small. There was slight wrist and finger drop on both sides, and the intrinsic hand muscles were notably wasted. The grip was poor, and there was well-marked intention tremor of the arms. The movements of his chest were good, the pulse 84, and the heart normal. His pupils reacted normally to light, and slight nystagmoid jerkings of the eyes were observed on lateral movement.

Sensation.—There was slight numbness of the finger tips, and he was apt to let small objects slip from his fingers, but there was no objective loss of tactile sensation or to pin-prick on the hands or arms, trunk, or feet and legs.

Reflexes.—Knee-jerks and Achilles-jerks absent. The plantar reflexes and all abdominal reflexes were also absent. There was no affection of the sphincters. His urine was normal. Electrical testing showed full reaction of degeneration in the leg muscles and in the extensors in the fore-arms.

Treatment by massage and galvanism to the muscles was given on alternate days, and he was given injections of strychnine twice daily, commencing with $\frac{1}{60}$ gr. and gradually increased to $\frac{1}{11}$ gr. after ten days. His condition remained much the same until May 6, when he had three bad attacks of choking. His pulse was irregular, its rate increased to 150 per minute, with respiration 36. He had considerable difficulty in breathing, and the diaphragm appeared to be paralysed. The strychnine injections were stopped, and morphia and atropine

were administered, but he never rallied, and he died at 3.20 on the following morning, May 7.

A necropsy was performed ten hours after death, and the following is a summary of the findings:—

A well-nourished man with several pedunculated fibromata on the skin of his back. The muscles of legs and hands were wasted. No thickening of the cutaneous nerves was noted. There was bronchopneumonia with racemose areas of peribronchial consolidation, surrounded by areas of collapse, in the lower lobes of the œdematous lungs, and parenchymatous degeneration of the liver, kidneys and myocardium.

Nervous system.—The brain, which was preserved unopened in 10 per cent. formol-saline, appeared normal externally. The cranial nerves were not noticeably enlarged.

Spinal cord in its membranes felt thick and elastic as if œdematous, and the meningeal vessels were injected. On opening the dura the thickening was seen to be due entirely to a great increase in size of the nerve-roots, especially those forming the cauda equina, which had a curious purplish colour. The posterior root ganglia were less conspicuous than usual. The left sciatic nerve was much enlarged, measuring 3·7 by 1·5 cm. at the level of the lower border of gluteus maximus muscle. It had a swollen, soft glistening gelatinous appearance. On section each individual fasciculus appeared changed to a clear, partly translucent cord which, although feeling soft, was tough to cut. The fibrous tissue in the nerve-sheath and that between the fasciculi appeared normal. A high bifurcation, shortly below the gluteus maximus, was present. The left median nerve showed similar changes.

The brain, spinal cord, sciatic and median nerves were preserved in 10 per cent. formol-saline. Frozen sections were stained with Sudan-III and hæmatoxylin, and by the Weigert-Pal and Bielschowsky's silver methods. Paraffin sections were stained with Ehrlich's hæmatoxylin and eosin, Weigert's iron hæmatoxylin and van Gieson's stain, Weigert's elastin stain and neutral red, Mayer's mucicarmine and toluidin blue for Nissl bodies. Some material was transferred to Müller's fluid, and after three months was embedded in paraffin and the sections prepared by the Weigert-Pal and van Gieson stains. Other blocks were fixed in Bouin's fluid and the sections stained by Mallory's acid fuchsin, aniline blue and orange G method.

Microscopical appearance. Sciatic nerve.—The epineural fibrous

sheath appears normal, but the interfascicular fibrous tissue contains thin collagen fibres separated more widely than usual by œdema.

The perifascicular sheaths are thrown into irregular folds owing to the shrinkage of their contents during the fixation and preparation of the sections. This shrinkage is a remarkable feature of the fasciculi. It causes diminution in size of the macroscopic specimen seen in the photograph of the Kaiserling preparation (fig. 1), where the nerve has shrunk from 3·7 to 2·2 cm. in width. It is most marked in paraffin material, but can also be seen in frozen sections. The folds are extremely irregular, giving the cross-sections of the bundles an appearance resembling a map of a rocky archipelago in which the islands have numerous capes and bays. A single fasciculus is seen in fig. 2. On the inner surface of the perineurium, and running from it between the nerve-fibres into the centre of the fasciculi, is a peculiar acellular clear material (*a* and *b*, fig. 2).

The amount of this substance varies in different fasciculi and in different parts of the same fasciculus. Often it is thick and dense at one side (*b*) and thinned out into strands at the other (*a*). There is always more at the periphery, where it may reach 100 μ in thickness, than between the nerve-fibres. This substance stains faintly blue with hæmatoxylin, pink with neutral red, yellow with Van Gieson's stain, bright pink with eosin, and orange with Mallory's stain. A few lamellæ in the more condensed portions can be stained with the Weigert-Pal method or with neutral red; hence it may be called amphophile, but its nature is quite unknown. The laminated appearance is probably an artefact due to fixation and dehydration. The substance is evidently the same as the clear interstitial substance described by Marie and Bertrand in their case [1].

Mixed with the amphophile substance there is a little mucinoid matter at the periphery of the nerve, and much more between the nerve-fibres. This stains with Mayer's mucicarmine in threads, as shown in fig. 4. There is also present a considerable amount of fluid coagulated by the fixative which scarcely stains. Thus the endoneurium is given an appearance similar to the subcutaneous tissues in myxœdema.

The most noticeable change in the nerve-fibres is the formation of several more or less concentric layers of fibres giving the remarkable "onion bulb" appearance described by Dejerine and most other authors; it can be seen in fig. 3. This seems to be due mainly to a proliferation of the sheath of Schwann and its cells. The cellular proliferation is very great. As in the normal nerve, there is only one

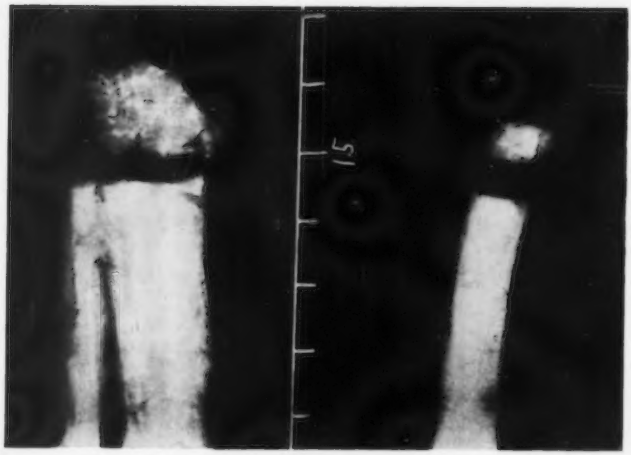


FIG. 1.—Photograph of the affected great sciatic nerve A, together with one B, from a normal fat man. The cross-section shown in each case is 1 cm. below the lower border of the gluteus maximus muscle. Scale in centimetres.

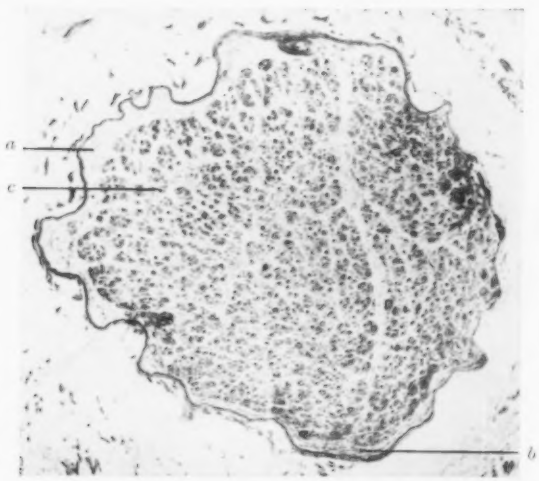


FIG. 2.—Low-power photomicrograph of one fasciculus of the sciatic nerve. It shows the irregular outline, peculiar interstitial substance, *a*, and the laminated appearance in the more condensed part, *b*. The few myelin sheaths remaining appear as dark dots, *c*. Weigert-Pal and van Gieson.

To illustrate Dr. Wilfred Harris's and Dr. Wilfrid D. Newcomb's article.

nucleated cell to each internode, the chance of seeing a nucleus in any cross-section is small, but here the average number of nuclei to any cross-section of a fibre is three, and frequently as many as six nuclei may be found around a single fibre.

It is difficult to be certain if all these laminæ are formed from the sheath of Schwann, or if the fibrous sheath of Henle also takes part. The outer layers are formed of collagen fibres which stain normally and have thin, elongated darkly-stained nuclei. The inner layers stain a brighter pink with eosin and have a yellower tinge with van Gieson's stain. Many of the nuclei are rounder, stain less deeply, and have a fine reticular pattern, resembling more closely the normal cells of Schwann. There seems little doubt that these central cells and fibres are formed from the sheath of Schwann, but whether the outer ones are of the same origin and older, or whether they are formed from the fibrous sheath of Henle, is not certain.

The myelin sheaths are usually destroyed. In several fasciculi none are present, but usually a few can be seen (fig. 2). The number varies considerably in different fasciculi. A few sheaths are practically normal, but most are in various stages of degeneration: some appear as thin or dotted rings, poorly stained by the Weigert-Pal method, others as thick, swollen club-shaped masses.

The axis-cylinders are difficult to demonstrate, and the preparations stained by Bielschowsky's and Malory's methods are not easy to interpret. In nearly all the fibres there is something stained by the silver which might be an axis-cylinder. Many of the larger "onion bulbs" contain several small fibrils, and others a large stained area. There are also a number of stained fibrils entirely outside the sheaths. These appearances have been interpreted as axons in various stages of degeneration and regeneration. As there is no sign of axonal reaction in the anterior horn-cells (fig. 8), it is unlikely that the axis cylinders of the motor nerves have been destroyed.

To summarize the main features of the sciatic nerve: Axis-cylinders are usually present, but the myelin is mostly destroyed; the neurolemmal sheaths have proliferated and formed "onion bulbs"; mucinoid and œdematous material is present between the nerve-fibres, and the fascicular sheaths are irregular, and contain the peculiar amphophile substance.

The median nerve shows a similar appearance, but the changes are less advanced. There is little of the peculiar amphophile interstitial substance, and when it is present it is confined to the periphery of the fasciculus just beneath the perineurium. The myxœdematous condition

of the endoneurium is well marked, and contains as much mucinoid material as the sciatic nerve. The "onion bulb" arrangement of the proliferated sheath of Schwann is present, but is not as prominent. A conspicuous feature is the variation in the amount of demyelinization in the different fasciculi; in some all the myelin has disappeared, while others contain nearly as much as normal and the sheaths themselves are thicker.

The posterior root ganglia were relatively inconspicuous. This is probably due to the increase in size of the nerves overshadowing the ganglia, which are not enlarged. There is no obvious lesion in the ganglia (fig. 9). Some cells are crenated, and in some the nucleus is excentric, but no stress can be laid on such changes in fixed dehydrated sections. Marie and Bertrand, 1918, and Souques and Bertrand [2], 1921, both describe these changes as significant, but they would seem more likely to be artefacts. The Nissl bodies appear normal. The nuclei in the pericellular sheath seem prominent, but they are just as numerous in a normal control. Ganglia from the lumbar, dorsal, and cervical regions were examined, and all were similar.

The nerve-roots examined all showed some degree of degenerative changes in the myelin sheaths and varying amounts of proliferation of the sheath of Schwann. There is considerable variation in different fasciculi of the nerves, and also from root to root, but on the whole the changes become more advanced from above downwards. Even in the cauda equina they are not nearly so marked as in the sciatic nerve. As a general rule the change is more pronounced in posterior than anterior roots, although this is not quite constant. None of the interstitial clear substance has been found in the roots, and only very small amounts of the mucinoid material. The fibrous proliferation around the fibres is present, especially in the lower roots, but the "onion bulbs" are smaller and thinner than those in the peripheral nerves. The changes in the myelin sheaths are very variable, but always there is less degeneration than in the corresponding peripheral nerves. Towards the upper end of the cord the myelin is frequently in irregular rod or club-shaped masses, with a small surrounding fibrous sheath. A similar change is present in the lower cranial nerves, being particularly well shown in the root of the vagus, where the thickness of the fragments of myelin is very striking. Several vagal fibres are completely demyelinated, as seen in fig. 7.

Unfortunately, neither the vagus nor the phrenic nerves were preserved, but as the changes in their roots are well marked, it may be assumed that both suffered similar changes to the median.

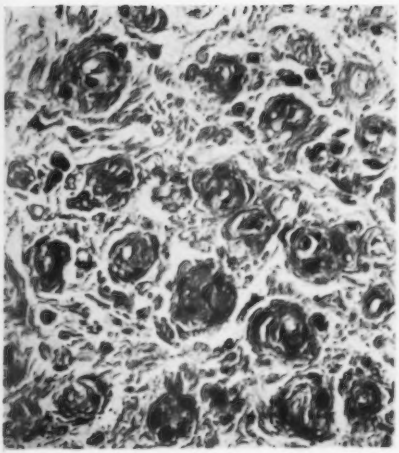


FIG. 3.—High-power view of a cross-section of the sciatic nerve, showing "onion bulbs" with interstitial substance between. Iron hæmatoxylin and van Gieson.

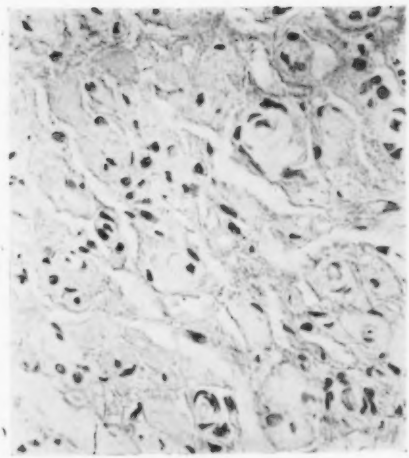


FIG. 4.—The same section stained with Mayer's mucicarmine. The strands of mucinoid material appear light grey.

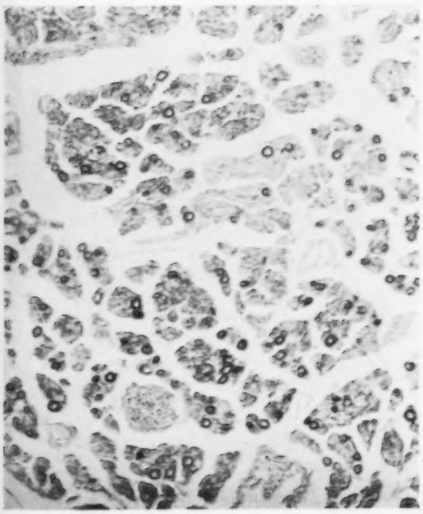


FIG. 5.—Cross-section of the posterior root of the fifth lumbar nerve, showing few medullary sheaths and much proliferation of the sheaths of Schwann. Weigert-Pal and van Gieson.

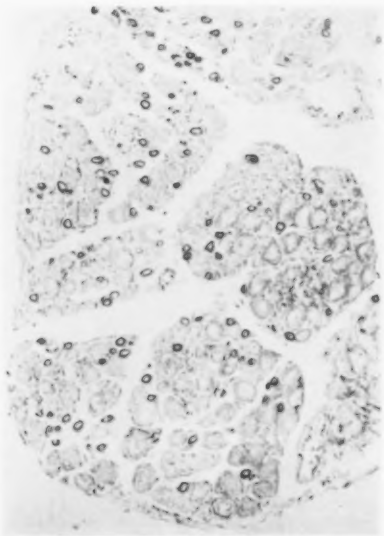


FIG. 6.—Cross-section of the anterior root of the first dorsal nerve, showing small "onion bulbs" and few medullary sheaths. Weigert-Pal and van Gieson.

FIG. 7.—Longitudinal section of the root of the vagus showing the black masses of degenerating myelin and grey areas of collagen fibres. Weigert-Pal and van Gieson.

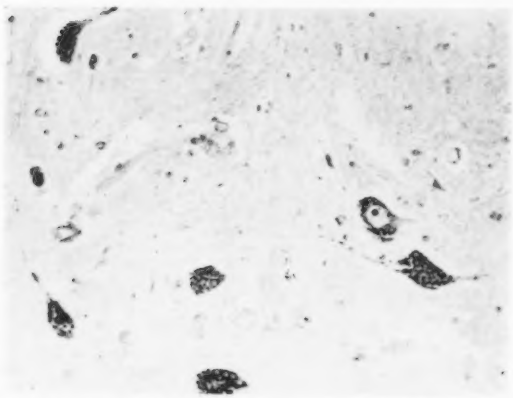


FIG. 8.—Anterior horn-cells of the second dorsal segment. (Normal.) Nissl method.

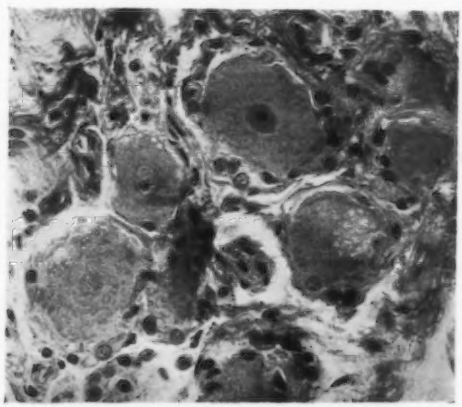


FIG. 9.—Mid-dorsal posterior root ganglion. (Normal.) Iron hæmatoxylin and van Gieson.

The highest root examined was that of the third cranial nerve; it shows the earliest lesions, viz., œdema separating the nerve-fibres and commencing fibrosis around them. It is noteworthy that here, where the change is just starting, there are only a few scattered lymphocytes present, no more than in a normal nerve. In fact, it may be stated that nowhere throughout the nerves examined in this case was there any sign of leucocytic infiltration, which agrees with most of the previous cases recorded, but Souques and Bertrand, 1921, lay considerable stress on the presence in their case of lymphocytes, plasma cells, and other wandering cells.

Where this case differs from all other necropsy records is in the spinal cord, which for the most part is quite normal. The dorsal and cervical regions show no signs of degeneration. In the lower lumbar region there is a vague thinning of the posterior columns in a Weigert-Pal preparation, as viewed with the naked eye. Microscopically the myelin sheaths in this area are in the form of dotted rings instead of complete annulets, but none have completely disappeared. As there is no sign of degeneration in Goll's column in the upper sections, it does not look as if any of the long ascending fibres in this part can have been destroyed.

The nerve-cells in both anterior (fig. 8) and posterior horns, as seen in Nissl and hæmatoxylin preparations, appear normal. The cells of Clarke's column also show no abnormality.

In sections at the level of the olive, the vagal fibres passing between the nuclei and the issuing roots appear normal, while immediately outside the medulla they commence to degenerate. This abrupt change coincides with the beginning of the sheath of Schwann and suggests that the essential lesion is its proliferation.

In this case there is no evidence of true inflammation. It would seem that the change is more in the nature of a hyperplasia similar to that seen in the breast in the so-called "chronic mastitis."

Recurrent attacks of polyneuritis without obvious cause, such as lead or alcohol, have been published by many authors, by Grocco in 1885, Ross and Bury in the case of two sisters, by Sorgo, by H. M. Thomas in 1898, in the case of a man, aged 28, who had five attacks of paralysis within six years, and by others (see *Brain*, vol. xlv, p. 427). In none of these, however, has hypertrophy of the nerves been discovered, except in the case described by Nattrass in a boy of 18, with double foot-drop, loss of the deep reflexes, and other signs of generalized multiple neuritis, in whom the nerve-trunks were palpable and

appeared to be enlarged. This patient had had two previous attacks of paralysis at the ages of 4 and 17. As this case did not end fatally, it is not possible to assume that the nerve-changes were comparable with those in our case.

It seems that the Dejerine and Sottas type of familial hypertrophic interstitial neuritis should be distinguished as a separate group from recurrent polyneuritis, to which our case appears to belong, though the interstitial hypertrophic neuritis found in the nerve-trunks and spinal nerve-roots in our case forms a remarkable link between the two groups, and it is conceivable that a similar underlying cause may be responsible for all of them, as an autotoxæmia from an enterotoxin, such as is the probable cause in hæmatoporphyrinuric polyneuritis.

In conclusion, we should like to express our thanks to Dr. J. G. Greenfield for his help in taking the photomicrographs.

REFERENCES.

[1] Marie, P., et Bertrand, I. *Annales de Méd.*, 1918, **5**, 209.
[2] Souques, A., et Bertrand, I. *Ibid.*, 1921, **9**, 305.

Notices of Recent Publications.

The Cytoarchitectonics of the Human Cerebral Cortex. By Constantin von Economo. English translation by S. Parker. Pp. 186, with 61 Illustrations. London: Humphrey Milford. 1929. Price 21s. net.

Notices of the German and French editions of this book have already appeared in this Journal and we now welcome an English translation. The design of the original has been hardly altered and the numerous whole-page illustrations are reproduced on almost the same page and in the same relation to the text as they occupy in the original book. We could wish, however, that the translator had not followed the original so exactly in some respects, as a too literal translation of the German has made the text either unintelligible or misleading in many places. For example, he speaks of a "clear nucleolus" and a "fat vacuole" in nerve cells. In fact it is often necessary to refer to the German or the French edition to arrive at the author's meaning. We could wish too that, instead of the long chapter headings of the original, the translator had adopted the useful paragraph headings of the French edition, which greatly excels the English edition both in the translation and in the reproduction of the plates. The latter fault is presumably due to the quality of the paper used, and may be improved in later printings, but it greatly detracts from the value of the book. In spite of these shortcomings, however, the book will be of value to many who prefer to have anatomical textbooks in their own language.

Tumours arising from the Blood-vessels of the Brain. Angiomatous Tumours and Hæmangioblastomas. By Harvey Cushing and Percival Bailey. Springfield and Baltimore: C. C. Thomas. Pp. 219 with 159 Illustrations. 1928. Price 34s.

This book deals with rare forms of tumour, of which the authors have only met with twenty-nine examples in a series of 1,522 intracranial tumours. Of these twenty-nine, six were venous angeiomas, nine arterial (arterio-venous) angeiomas, one a telangiectasis and thirteen hæmangeioblastomas (plexiform angeioma). It is remarkable that all the venous angeiomas were supratentorial, and all the hæmangeioblastomas subtentorial. This must be considered purely fortuitous as regards the venous angeiomas, as cerebellar or pontine examples are not uncommon, but it agrees with the experience of most other observers, especially Lindau, who could find no example in the literature of a supratentorial hæmangeioma.

The first half of the book deals with the arterial and venous angeiomas and the case of telangiectasis. None of these cases has been very favourable for operation. In one case of arterial angeioma and one of venous angeioma the tumour was successfully removed and several other cases appeared to be benefited by simple decompression, or by ligature of arteries in the neck. X-ray treatment was used in most cases but proved of doubtful value. On the whole the authors recommend simple decompression for these classes of tumour.

The second half deals with the cerebellar hæmangeioblastomas. Of these seven were in the walls of cysts, and the other six were rather large solid tumours. In this class of growth the operative mortality was high, as four patients died within forty-eight hours of operation. But in four cases complete, and in three cases partial, removal of the growth was successfully performed.

In discussing diagnostic and therapeutic possibilities in relation to the venous, arterial and telangiectatic forms, the authors comment on the difficulty of a pathological diagnosis and the impossibility in the majority of cases of dealing with the disease in a radical manner. In the cerebellar hæmangeioblastomas also it was impossible at the time when the patients came under observation to form an opinion as to the nature of the growth, although a later examination of one patient revealed a retinal angeioma and family history of similar cerebellar disease.

In dealing with so rare a type of tumour the authors have taken the only possible course in writing a monograph rather than a textbook. Full reports are given of a large proportion of the cases, and the literature dealing with the subject is fairly exhaustively surveyed. Altogether it is a useful and informative book; perhaps most useful in being largely a record of unexpected difficulties met at operation, and of wise retreat when advance appeared too hazardous. As minor criticisms we note that the common picro-fuchsin counterstain is always spelt "van Giesen," and that the authors persist in the use of the name "meningioma" in spite of a general agreement that the name of a tumour should be taken from the tissue, and not from the anatomical structure, from which it arises.

Epilepsy, from the Standpoint of Physiology and Treatment. By W. C. Lennox and Stanley Cobb. Pp. 197. London: Baillière, Tindall and Cox. 1928. Price 16s.

This monograph is a critical survey of our present knowledge of the nature of the pathogenic factors concerned in the occurrence of epileptic seizures, whether associated or not with any demonstrable structural disturbance in the central nervous system. The authors' own investigations, valuable though they be, take a subsidiary place to the review of observations and theories, old and recent, which have been put forward by others. The only criticism of the book that can be suggested is, in fact, its comprehensiveness; even the

views of abdominal surgeons and of non-professional bacteriologists are included, for the aim of the authors is to assimilate all available evidence.

The interesting critical review of the neurological mechanisms of convulsions includes the irritation, release, "short-circuit" and explosive theories, one of which alone is regarded as sufficient, though it is suggested that the explosive theory, according to which the seizures result from some sudden metabolic change in the nervous system, may finally explain the epilepsies. Functional abnormalities in the nervous tissues of a physico-chemical nature, as disturbance in oxygen consumption, ionic equilibrium, hydrogen-ion concentration and in the permeability of the cell membranes, are also fully considered, but the present state of our knowledge does not permit even tentative conclusions as to the part these play. A search for the exciting causes of seizures in abnormalities in other systems, in metabolism and in the acid-base relationships, occupies the greater part of the book; the profusion of theory and the poverty of definite facts, so prominent in the literature of epilepsy, is strikingly illustrated in these pages, but the critical study of these subjects which the authors give us will be extremely useful to all interested in the subject. They personally find the essential elements in the precipitation of the seizures to be "oxygen lack," alkalosis and a disturbance of the water-balance of the tissues. Further investigation will determine the importance of these and other factors, but it is to be hoped that the innate or acquired disturbances in the brain that the authors admit to exist in all cases in which the epilepsies occur, will not be lost sight of. Many changes in the fluids of the body can excite convulsions in both the normal and predisposed, but there is as yet no compelling evidence that in epilepsy the immediate as well as the predisposing cause of the seizure does not lie in the brain.

Die Vorder- und Mittelhirnganglien des Menschen als plastische Gebilde. Von B. SCHLESINGER. S. 55. Berlin: J. Springer. 1928. Price M. 6.60.

The anatomy of the internal structures of the brain is usually studied in sections through it, and their topographical relations are learned by a mental piecing together of sections in different planes. Reconstructed models in wax and other substances may be, however, employed for teaching purposes, but it is obviously preferable to demonstrate these structures in preparations of the brain itself. The author describes a series of dissections by which this can be done, describes and figures the preparations, and supplies a series of stereoscopic photographs of them which should be valuable in the teaching of students and in a revision of the anatomy of this complicated region.

Anatomy and the Problem of Behaviour. By G. E. COGHILL. Pp. 113. Cambridge: The University Press. 1929. Price 7s. 6d.

This book is based on a correlated series of studies on the development of behaviour and on the growth of the nervous system in an amphibian,

Amblystoma. The simplest reactions of the embryo from the egg stage are first described, and later the swimming mechanism, the movements and local reflexes of the limbs. Terrestrial locomotion and the feeding reactions are also analysed in relation to the structure of the maturing nervous system. The embryo is, however, perfectly integrated before it possesses a nervous system, and the second chapter deals with the dynamic antecedents of the neural mechanisms, as the appearance of polarity and of the so-called metabolic, axial and other "gradients," and their influence on the developing nervous system, the paths of which are determined largely by the preneural activity of the tissues. In the final chapter on the growth of the nerve cell and the interpretation of behaviour, emphasis is laid on the view that behaviour does not depend merely on a combination of reflexes, but that there is an organic unity from the beginning, in fact the central mechanism of a reflex is developed long before the reflex itself appears.

How to Stain the Nervous System. By J. ANDERSON. Pp. 139. Edinburgh: E. and S. Livingstone. 1929. Price 5s.

The only textbooks on the histological examination of the nervous system in English are either too detailed for the novice, or do not include some of the most recent methods of staining. This small book by the chief Laboratory Assistant at the National Hospital is consequently welcome and will be of the greatest value to the laboratory technician as well as to the student of neuropathology. All the methods described in it have been used by the author in his routine work, some of them or modifications of other methods have, in fact, originated from him, and they can therefore be accepted as the most suitable and reliable now available. They are all described clearly and concisely, and a short résumé follows the detailed description of each procedure. In addition to staining he deals with the best means of preparing the tissue, of cutting sections, of obtaining serially stained sections, and other procedures which have been evolved from a long practical experience.

Handbuch der Geisteskrankheiten. Herausgegeben von OSWALD BUMKE. Erster Band: Allgemeiner Teil, I. S. 732, mit 44 Abbildungen. Price RM. 68.80. Dritter Band: Allgemeiner Teil, III. S. 333, mit 77 Abbildungen. Berlin: Springer. 1928. Price RM. 34.40.

This System of Psychiatry will probably take the place which Aschaffenburg's notable "Handbuch" has occupied for the last two decades. Unlike the latter, it has no Swiss or Austrian contributors; it is wholly German, but it is none the less complete or distinguished for that.

The general tone of the work is indicated by the Editor's introductory article on the aims, ways and limits of psychiatric research. Bumke considers

psychiatry as essentially one of the natural sciences, calling for an exact essentially objective determination of facts and for strict logical reasoning: it must not set about translating into the language of neurology or cerebral pathology psychological facts whose physiological correlates are unknown, nor must it deal in the "metaphysical-romantic." The "neurologizers" he handles rather kindly, but at the psycho-analysts he girds with caustic vigour. His survey is wide and severely critical.

The history of psychiatry is dealt with by Birnbaum; he gives little attention to other than German schools, but this proves to be no impediment to the lucid setting forth of the main lines along which psychiatric thought and research have travelled.

The next section, on Inheritance, by J. L. Entres, is a monograph of great thoroughness; it professes to be no more than a compilation, but in this confused field a faithful inquiry into all that has been written and an ordered presentation are of great value.

A brief survey of acquired somatic causes by Korbsch is followed by articles on external psychic causes and on structural analysis by Kehrer, with a useful appendix on the anamnesis. These end the section on etiology. The rest of the volume is given up to general symptomatology.

The pathology of perception is dealt with exhaustively in two papers by Stein and Mayer-Gross, whose original work in this connection has been so distinguished. Disorders of memory are discussed by Kurt Schneider, disorders of thought by Jahreiss, who also deals with disorders of consciousness. Kretschmer's comprehensive yet brief consideration of disturbances of affective life, and Stertz's article on disorders of intelligence conclude the volume.

The other volume published deals with the bodily changes that may be associated with mental disorders. It is fittingly introduced with a balanced account of what is known as to the relation between physique or habitus and psychic predisposition—a field in which much work is being done in Germany and America, and in which extravagant claims are sometimes made. Neurological changes in mental disorder are described by Rosenfeld almost too thoroughly; one has at times the impression that one is reading a somewhat long-winded textbook of neurology, but at any rate nothing is omitted. Küppers writes on the pulse, blood-pressure, vasomotor changes and distribution of blood; Wuth resumes what had been learnt about body-weight, the endocrine system and metabolism in this connection by 1926, when the article was written; and with Kafka's authoritative paper on humoral pathology, a valuable addendum to his monograph in "Aschaffenburg," the volume ends.

One cannot summarize contributions of such scope as these, nor profitably discuss them, in a brief review. The work as a whole is admirable, well-proportioned and trustworthy. If one may judge by the two important volumes so far published, Prof. Bumke's hope that it shall give as complete an account as possible of the present state of our knowledge, and at the same time help towards attaining a new and higher standpoint, seems likely of fulfilment.

Die Gegenwärtigen Strömungen in der Psychiatrie. Fünf Vortrage von OSWALD BUMKE. S. 111. Berlin: Julius Springer. 1928.

The five papers here collected were written for various gatherings between 1924 and 1927, and make Professor Bumke's conservative position clear. There is of course some repetition, but on the whole one finds a discerning survey of the various tendencies in psychiatry now and during the last few years.

The treatment is rigorously critical, especially in the numerous passages devoted to psycho-analysis; onslaughts with horse and foot follow tempered, even niggardly, appreciation.

The little book is attractively written and is well worth reading as the expression of wide knowledge and a clearly-defined point of view.

Subordination, Autorität Psychotherapie. Von ERWIN STRANSKY. S. 69. Wien: J. Springer. 1928.

The relation of patient to doctor has been studied closely by Freud and his followers, and in the word "transference" much fundamental psycho-analytical doctrine is implicit. Professor Stransky, writing as a "clinical empiricist," joins issue with the Freudians. It is essentially, he maintains, the relation of subordination to authority, a "transsexual" matter, that is concerned. He reviews education, religion, government, social life and authority in general in this light, and sets forth a method of psychotherapy for which he claims good results. He remarks justly that time-consuming methods such as analysis cannot be applied to large numbers of patients, and offers a substitute that is not exclusive of other therapeutic measures. His method, however, does not differ in practice from that of many psychiatrists untroubled by theories which assert a dominance over the patient and make use of the situation of dependence thus brought about, without being able to manage or dispose of it other than crudely. This crux the writer does not elucidate.

The critical and casuistical passages are interesting but not convincing.

Two Essays on Analytical Psychology. By C. G. JUNG. Translation by H. G. and C. F. Baynes. Pp. 280. London: Baillière, Tindall and Cox. 1928. Price 10s. 6d.

These essays, much altered from the first edition which appeared in 1916, are written for the "cultured layman," and it is to him that they may be expected to appeal. Speculation of this sort is fascinating, no doubt, and stimulating: but it cannot sufficiently account for its evidences even when it professes to be based on clinical experience. This book is, however, excellent as a literary work, lucidly presenting difficult, if not mystical, conceptions and provoking thought; one can understand why so many of Jung's non-medical adherents are evangelists of a cult.

The translation is faithful and clear, but the translator's preface contains an unfortunate mixture of adulation and misstatement. Jung is a distinguished psychiatrist; he is not Sakyamuni.

Practical Clinical Psychiatry. By EDWARD A. STRECKER and FRANKLIN G. EBAUGH. Second Edition. Pp. 458. London: H. K. Lewis and Co. 1928. Price 18s.

This is a useful compendium of psychiatry as currently taught in America. It is presented chiefly in the form of case-histories and discussions, with brief formal accounts of diagnosis, treatment, &c. It is clearly not intended for psychiatrists so much as for medical students and general practitioners. It is usually sound and reflects in the main Adolf Meyer's teaching. Occasional statements, such as those regarding the superiority of luminal to bromide in the treatment of epilepsy, or the assertion that in morphine addiction "the hyoscine treatment has proven of value in replacing the narcotic" are open to considerable objection. The frequent use of the word "præcox" as a noun and as an adjective synonymous with schizophrenic is irritating.

Die Psychosen der Schwachsinnigen. Von RUDOLF NEUSTADT. S. 188. Berlin: Karger. 1928. Price RM. 15.60.

The relative poverty of content in the psychoses of mentally defective persons has probably been the main reason why so little investigation into them has been made. Kraepelin's views on "Pfropfhebephrenie" stimulated interest in the relation of dementia præcox to congenital mental defect, but it is only recently that much attention has been paid to the whole subject. It is obviously one of considerable importance, not only on psychiatric grounds but also in its social, especially eugenic, implications.

The author states the evidence which he has required before deciding that feeble-mindedness, a condition of "stationary intellectual defect," was present; he has examined 209 such cases in which psychosis occurred, and by psychosis he understands "morbid, i.e., foreign and novel, psychic phenomena through which the individual line of psychic development is interrupted, temporarily or permanently." The histories of thirty-three of the patients are given in some detail; in a few of these the diagnosis of mental defect is not beyond cavil, but unless he has restricted his investigations to incontestable idiots such doubts could not well be avoided.

He deprecates the assumption that schizophrenia often develops in mentally defective persons; he holds that it is very rare and that in many supposed cases schizophrenic symptoms have appeared at so early an age that they have been regarded as evidence of mental defect, or that the latter diagnosis has been made on the ground of social maladaptation rather than of proven intellectual defect. He is inclined with his teacher Sioli to group together all the conditions he describes and to regard them as a special form of exogenous psychosis, conditioned by the exogenous factor, mental defect—in short mental defect indicates "not a disposition to any possible psychosis but only a specific disposition to the episodic psychoses here described."

Die psychopathischen Persönlichkeiten. Von KURT SCHNEIDER. S. 86. Leipzig und Wien: Franz Deuticke. 1928.

The first edition of this valuable work appeared in 1923; since then investigations into personality and character have been so numerous and fecund that much has been added to the first section of the book, dealing with general considerations, and much made more precise.

All psychopathic personalities are regarded by the author as abnormal in the sense of being different from the average, rather than different from a teleologically conceived ideal norm. They either suffer from their abnormality, or cause suffering to society through their abnormality. The implications and difficulties of this conception are discussed fully, the delimitation of psychopathic personalities from psychoses briefly sketched. Development, somatic basis (chiefly in connection with the doctrines of Kretschmer and of the brothers Jaensch) and the grounds for systematic subdivision are dealt with lucidly and carefully. The second part of the book is descriptive, with appropriate notes on the social significance, relation to psychoses and treatment of the varieties of psychopathic personality.

The book is admirably concise and restrained; it gives a complete picture, according to current German psychiatry, of the people who fall short in their human relationships.

Die Störungen des Bewusstseins. Klinish-diagnostische Studien von Prof. M. ROSENFELD. S. 247. Leipzig: Georg Thieme. 1929. Price M. 18.

This is a careful account of the disorders of conciousness. The author insists that all psychopathological phenomena must be observed and evaluated in immediate reference to the whole psychic state, i.e., the state of consciousness; much is therefore subsumed under this heading.

In a chapter on the manisfestations of unconscious psychic happenings it is pointed out that psycho-analysis can investigate the content of delusions and hallucinations and the relationship of these to experiences that have become unconscious, but that for a diagnostic judgment it is the manner in which they come and go and the patient's reaction to them that are decisive. "It is not what the patient says or hallucinates or dreads that matters, but how he experiences these happenings."

In an interesting discussion of the connection between cerebral processes and disorders of consciousness, the author goes into the problem of sleep and the mode of action of narcotics; he mentions, and is evidently rather taken with, Semon's assumption of an irritable substance in the cerebral cortex.

In the general symptomatology, besides the psychic manifestations, neurological and general somatic concomitants are dealt with systematically. Then follows the description of the pictures seen in special disorders. The author incidentally defines his attitude towards such matters as the distinction

between "psychogenic" and "hysterical" disturbances, and the diagnostic criteria of manic-depressive insanity and the schizophrenic group.

There are numerous references and a good index.

Psychologie. Von HARALD K. SCHJELDERUP. S. 330, mit 20 Figuren im Text. Berlin: Walter de Gruyter and Co. 1928.

This is a translation into German of a recent work by the Professor of Psychology at Oslo University. He has set himself the task of combining the findings of the various schools and giving an integrating survey in which "the more classical experimental psychology shall be fused with the results of behaviourist studies, as well as with those of psycho-analysis, into an organic unity." Watson and Freud, therefore, bestride the book: the harmony is not always satisfying. The author does not neglect discussion of other recent work, though one looks in vain for an appreciation of Pawlow's researches or of Spearman's.

The book is divided into sections, on the original equipment, the mnemic functions, and the personality and its conflicts, with a final summary of the practical applications of psychology.

The author is evidently widely read, but appreciative rather than discriminating: he is constantly mindful of the human being he is writing about, and so his book remains interesting and relevant: he often adduces psychopathological problems and illustrations. The exposition throughout is lucid and consecutive.

A Study of Intercranial Surgery. By HUGH CAIRNS. Pp. 83, with 30 plates. London: H.M. Stationery Office. 1929. Price 3s.

This brochure, published by the Medical Research Council, contains the impressions of a student gained during a year spent with Dr. Harvey Cushing. His aim is to recount the methods employed in this clinic in the diagnosis and treatment of intercranial tumours; he contributes nothing new to the subject, nor attempts a critical review of the many problems that it presents. He records the case histories of 32 patients, some of which had been previously published, in order to illustrate the difficulties of diagnosis and the surgical methods employed in their treatment. Thirty plates are appended containing a large number of figures, some of which have been printed before, but many are only reproductions of temperature and other charts after operations, or photographs of healed wounds.

The Child of Circumstance. By ALBERT WILSON. Pp. 420. London: John Bale, Sons & Danielsson, Ltd. 1928. Price 15s. net.

The increase of interest in criminology is evidenced by the numerous books that have been lately devoted to it, chiefly from the psychological side. The late Dr. Wilson devoted much time to its study, though from the humanitarian

rather than the scientific side, and has published several books and articles relating to it. This volume scarcely substantiates his claim to deal with the criminal from a scientific point of view, for it shows little insight into many of the problems crime and the criminal present, but it is readable and recounts interesting observations in a clear and intelligent form. It is unfortunately diffuse, including chapters on Lord Lister, Quakerism and other matters that are really not relevant, while there is too much theorizing on pathological and biological problems involved, and a striking neglect of recent investigations.

Mikroskopische Anatomie des Vegetativen Nervensystems. Von P. Stöhr, Jr. S. 251 mit 243 Abbildungen. Berlin: J. S. Springer. 1928. Price 36 M.

The vegetative nervous system will certainly in the future occupy a more important place in clinical medicine than that at present allotted to it, and a more exact knowledge of its anatomy must precede any attempt to establish a rational pathology of it. We have been for long acquainted with the topography and distribution of its main tracts, and from the work of Langley and others, with the chief principles of its construction, but our knowledge of the peripheral distribution of the sympathetic and parasympathetic fibres to various organs of the body has been patchy and dependent on numerous separate articles widely scattered throughout the literature. In this beautiful monograph Stöhr has furnished a comprehensive account of all the elements of the vegetative system, and illustrated his descriptions by numerous figures, both original and borrowed, some of them in colour. The excellent reproduction of these illustrations is one of the features of the book that deserves the highest praise.

The nerve-supply to the blood- and lymph-vessels, to the endocrine glands and smooth muscles, as well as to the various visceral organs, is described in detail in separate sections. Preceding work is liberally but critically reviewed, and in many instances the physiological significance of the anatomical arrangements is discussed. The volume can be strongly recommended as a classical textbook and as a useful work of reference.